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THE MONTH

IN many ways the most striking advance in medicine in recent years has been our greater understanding of fluid and electrolyte control in the body. This has inevitably involved an intensive study of renal physiology. Much of this information is still scattered in the pages of specialist journals and monographs and is therefore lost to the majority of clinicians. It is for this reason that we have chosen 'Current concepts of renal physiology in health and disease' as the subject of the introductory article in our symposium on 'Renal Disease' this month. Dr. Lewis's article on this subject, together with Professor Bull's on 'Anuria and its management', demonstrates well the tremendous progress that has been made in the last decade. The impact of advances in treatment in the same period is equally impressive as shown by Dr. Arneil's article on 'Nephrosis and its management' and that on 'The management of genito-urinary tuberculosis' by Mr. Band and Dr. Murray. That modern therapy, however, is not without its hazards is evident from Dr. Robson's review of 'Drug-induced renal disease'. The radiologists have not been lagging in their efforts to enhance the value of their specialty in diagnosis, as is well brought out by Dr. Stevenson in the final article on 'The present status of renal radiology'.

The Symposium

WHY so much unnecessary noise has been tolerated for so long in so many different hospitals is one of those mysteries of life that the ordinary individual will never be able to understand. As the King Edward's Hospital Fund for London has recently demonstrated at Paddington Hospital, the problem can be largely solved with a modicum of common sense and a minimum of financial expenditure. The simple procedure, as outlined in the Fund's annual report for 1957, was to find out from the patients what noises worried them. The hospital secretary then got busy. 'He found a simple method of stopping the bed screens from rattling and banging. He had all the doors oiled and all the automatic shutting devices repaired. Every trolley wheel was cleaned, oiled and, if necessary, re-tyred; a new material for dressing-trolley tops was discovered which deadens the rattle of equipment. Arrangements were made for all new student nurses to be visited in the hospital by a shoe manufacturer who fitted them with quiet comfortable shoes'. The cost of all this was trivial.

Noise in Hospital

Now that it has been demonstrated that the administrators can do so much to solve the problem, there remain two causes of noise for which the doctors must find a remedy: the noisy patient and the patient who snores. As the

King's Fund points out, both of these would be remedied by the installation of cubicles, but this is both expensive and administratively difficult. Is it really beyond the wit of the medical profession to produce a more practical solution? With the noisy patient there should be little difficulty in view of the large range of sedatives and hypnotics now available to the profession. But what about the patient who snores? There are traditional remedies galore, but it must be confessed that hitherto the medical profession has tended to look upon snoring as more of a music hall joke than a problem for serious investigation. It is therefore satisfactory to know that the King's Fund is encouraging an experimental investigation of the subject. We trust that in this worthy work they are receiving the full support of the Clinical Research Board of the Medical Research Council and the College of General Practitioners, for the patient who snores can be as serious a problem in general practice as in hospital practice.

Public Health in France

SOME interesting differences between the public health services in France and in this country are noted by J. S. Cookson (*Publ. Hlth* (*Lond.*), 1958, **72**, 179) who has made a special study of the former. In France, a premarital examination, including special examinations for syphilis and tuberculosis, is compulsory. An unsatisfactory examination is not a bar to marriage but the certificate, which gives no diagnosis, must be delivered to the official at the registry office. When the birth of a child is registered the mayor presents the parent with a 'carnet de santé'. This is a booklet in which the health visitor records the progress of the child, including dates of inoculation and the like. Vaccination against smallpox is compulsory within the child's first year. Combined inoculation against diphtheria and tetanus is also compulsory—between the ages of 12 and 18 months.

Although, in Dr. Cookson's opinion, the French school health service is not so well developed as ours, there are certain aspects of it which we might well emulate. One, which Dr. Cookson quotes with approval, is that there is one comprehensive service covering both school and university, thereby ensuring continuity of medical supervision through all stages of education. Equally commendable is the rule that no child is allowed to start at school unless he has been vaccinated against smallpox and immunized against diphtheria. All children are examined annually at school and, though this may take place at speed (30 an hour or 120 a day), Dr. Cookson was impressed by the fact that, in the examinations he witnessed, the doctor insisted on each child being stripped. Incidentally, although many of the children he saw came from poor homes, he saw few flea bites or verminous heads. After every examination the parents of each child receive a personal letter, even if all is well. An advisory service is provided for those parents who wish advice on what careers the children should adopt when they leave school at the age of 14. When Dr. Cookson visited the advisory centre at Soissons he was told by the psychologist in charge that in France girls wish to become

good wives and mothers, so they prefer good domestic training. Apparently, in spite of all its political and economic vicissitudes, the traditional French gift for putting first things first is still as strong as ever.

Latch-Key Children

LATCH-KEY children was the apt term used in a broadcast towards the end of 1956 to describe those children whose mothers provided them with a latch-key when they went out to work. In order to determine to what extent these children constituted a problem in Middlesex, the principal school medical officer carried out a survey, covering 153 schools of all types, attended by over 60,000 children. The results of this survey are contained in his recently published annual report for 1957 and show that latch-key children constituted 37 per cent. of those attending grammar schools, 44 per cent. of those attending secondary schools, 23 per cent. of those attending junior schools and 7.5 per cent. of those attending infant schools.

In the opinion of the head teachers of these schools, the personality of the parents, rather than whether or not the mother was at work, lay behind child neglect. On the other hand, there was considerable criticism of mothers whose work did not coincide with school hours and who continued to work during school holidays. Amongst other things this involved children being sent to school who were not fit to be there, the inability of sending home children who became ill during school hours because there was no-one at home, and a tendency to keep older children at home either to look after sick smaller brothers or sisters or to perform the necessary house chores. Although in the main there was little evidence of physical suffering among the children, there was a proportion who were grubby, tired and listless, or emotionally disturbed. It is judicially concluded that 'what has emerged is that nobody really knows whether or not the fact that the mother of a family goes out to work is harmful', and the challenging question is asked: 'Has everyone accepted a perhaps inevitable trend of modern life as something harmful because it is new and different?'. It is simply evading the issue, however, to say that 'a bored, cross and nagging mother in the home can surely do more harm than a cheerful, good-natured one who goes out to work', and there will be many more who will be in agreement with those head teachers who 'emphasized the need for the education of parents in the preservation of family life and in the dangers likely to result from leaving children alone for long hours or roaming the streets and joining street gangs'.

Involuntary Laughter

INVOLUNTARY laughter is one of the curiosities of neurology which has aroused considerable interest in recent years. In reporting a case in a young man which was cured by removal of a neurofibroma of the fifth cranial nerve, M. W. Wood and his colleagues (*Proc. Mayo Clin.*, 1958, **33**, 266) provide a useful summary of the available information on the subject. They classify it into two main forms: one associated with epilepsy and the other occurring

without associated effect in a setting of intact consciousness. It can result from varied lesions, ranging from 'the limbic system at the cortical level through hypothalamic centres to the bulbar systems'. In other words, there is no evidence to suggest the existence of a 'laughter' centre and the precise cause in the individual can only be determined by careful investigation. The condition is quite distinct from emotional lability or emotional incontinence. The latter is merely a difference of degree, rather than kind, whereas the patient with involuntary laughter is 'the dispassionate witness to a complex motor act which normally would be the external manifestation of an inner affective state'.

One of the most interesting recorded cases is that of the patient undergoing removal of a papilloma of the choroid plexus under local anæsthesia. Every time blood was swabbed from the floor of the third ventricle the patient suddenly laughed, whistled and made obscene remarks. At necropsy the third ventricle was found to be filled with blood. One case has been recorded of sustained hilarity in a 58-year-old woman terminating in death. Here again the third ventricle was found filled with blood, which had apparently originated from a branch of the posterior communicating artery. The hæmorrhage had extended into the basal ganglia and both thalami. Yet another case worthy of note is that of the 75-year-old man who was seized by an attack of uncontrollable laughter while attending his mother's funeral. He had three such attacks and later died suddenly. Necropsy revealed a large ruptured aneurysm at the bifurcation of the basilar artery. This extended into the interpeduncular space, compressed the corpora mammillaria, and elevated the anterior part of the floor of the third ventricle.

Viscount Bracken

It is with a sense of deep personal loss that we have to record in these pages the death, on August 8, of Viscount Bracken. It is exactly thirty years since the company of which he was chairman acquired *The Practitioner*, and never once did his interest in it lag. In spite of all his many interests—in Church, State, education and the City—he always maintained a close personal interest in the journal. There were times in these latter years when he obviously felt that we were not adopting a critical enough approach to 'nationalized medicine' but, as every editor with whom he worked can bear witness, he never interfered with policy. His was a complex, ebullient personality. To sit up into the small hours of the morning listening to him

> 'talk of many things:
> Of schools—and art—and Fleet Street lords—
> Of bishoprics—and kings'

was an experience never to be forgotten. We who had the privilege of working with him mourn the loss of one to whom we could ever turn for help and advice and who was loyal to the end.

CURRENT CONCEPTS OF RENAL PHYSIOLOGY IN HEALTH AND DISEASE

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KNOWLEDGE of the function of the kidney has increased greatly in recent years, and a vast literature has collected. References are given here only to a small number of reviews of the subject which are readily available, and which refer to the original articles.

THE RENAL VASCULATURE AND THE RENAL BLOOD FLOW

The renal vasculature (Smith, 1956).—The interlobar arteries radiate outwards through the cortex giving off the afferent glomerular arterioles, each of which divides into the capillaries of a glomerular tuft; these reunite to form the efferent glomerular arteriole, which breaks up into capillaries forming a plexus round the renal tubules. The juxtamedullary glomeruli differ from the others, in that their efferent arterioles are wider and descend into the medulla as the vasa recta between the loops of Henle before turning backwards into the cortex.

The renal blood flow (Winton, 1956).—In perfusion experiments this remains constant over a wide range of perfusing pressure; either there is autoregulation of the renal vessels or the distribution of the blood within the organ must vary with different flows. It has been found that the hæmatocrit of the blood in the whole kidney is lower than that of aortic blood and that red cells traverse the organ more rapidly than plasma; it has therefore been suggested that separation occurs so that red cells take a shorter path, through juxtamedullary glomeruli, while the plasma flows mainly through those in the cortex. Changes in this distribution would cause variations in the resistance offered to blood flow at different pressures. Renal vasoconstriction is produced by many influences, including emotion, adrenaline, anæsthesia, surgical procedures, intravascular hæmolysis and the fall of cardiac output resulting from standing upright or from hæmorrhage. It may be extreme if the latter is severe. Homer Smith quotes figures in which a fall of cardiac output from 5.3 to 3.75 l./minute was accompanied by a fall in renal blood flow from 1,200 to 160 ml./minute. This response may not occur during anæsthesia. Renal hyperæmia occurs during pyrexia and may be produced by certain drugs such as hydrallazine; it does not result from renal denervation or spinal anæsthesia.

Moderate anæmia or polycythæmia cause little change in renal *plasma* flow (RPF). When the hæmatocrit is raised by transfusion in a case of chronic renal failure with anæmia, the normal renal vascular response may not occur and renal function may unexpectedly deteriorate (de Wardener, 1956).

GLOMERULAR FILTRATION

Electron microscopy has revealed the complex structure of the glomerular tufts (Smith, 1956). The endothelial cell of the capillary is applied to a fenestrated membrane (the holes being 400 to 900 Å wide) attached in turn to a basement membrane (lamina densa) which may have holes up to 100 Å across. Applied to the outside of this are the innumerable interdigitating processes (pedicels) of large cells called podocytes, so that only about one-tenth of its surface remains uncovered; presumably the water of the plasma in the glomerular capillaries filters through the holes in the membranes and between the pedicels to the capsular space; some escape of proteins would also be possible, and it is now accepted that glomerular filtrate contains these in amounts similar to those in the cerebrospinal fluid. Recent work, however, has cast doubt on the existence of all these 'holes' and the nature of the filtration process remains uncertain.

The glomerular filtration rate (GFR) averages 124 ml./minute in normal man. The filtration fraction (the ratio GFR/RPF) tends to vary with fluctuations in renal blood flow so that the corresponding changes in GFR are smaller. The GFR is therefore normally stable; the evidence is strongly against the volume and composition of the urine being regulated by GFR changes.

TUBULAR REABSORPTION AND SECRETION

From the capsular space, the filtrate passes down the lumen of the proximal tubule, where all the protein and glucose, about 80 per cent. of the electrolytes and, probably, some 40 per cent. of the urea are reabsorbed. A large part of the water of the filtrate is also reabsorbed to maintain osmotic equilibrium with the plasma.

When the amount of glucose filtered is increased by raising the blood level, the rate of tubular reabsorption increases up to a maximum (Tm, in mg./minute) above which the excess appears in the urine. Normally this does not occur until the plasma level exceeds 180 mg./100 ml., but in some otherwise normal subjects the Tm is low and glucose is found in the urine at lower plasma levels (*renal glycosuria*). Proteinuria occurs when there is a great increase in the amount filtered, either through abnormal glomeruli, as in renal disease, or when there is a rise in renal venous pressure (the probable cause of postural proteinuria).

Normally, about 20 ml. of fluid are delivered to the distal tubule every minute. It is here that the final elaboration of the urine occurs, by means of several remarkably selective and flexible processes. Sodium ions can be

reabsorbed, almost completely if necessary, by the action of adrenal steroids, which increase the excretion of potassium. Sodium ions are also exchanged directly for either potassium or hydrogen ions, the latter being derived from the ionization of carbonic acid, formed in the tubular cells from carbon dioxide, a reaction accelerated by carbonic anhydrase (fig. 1). The net result is that sodium and bicarbonate ions are transferred to the blood and potassium and hydrogen ions to the urine. The latter are excreted partly in the free state, producing an acid urine (the minimum pH being about 4.6), are partly buffered by HPO''_4 ions to form $H_2PO'_4$ and are partly combined with ammonia formed in the tubular cells themselves. The production of the latter can be greatly increased when large quantities of acid have to be excreted while fixed base has to be conserved, as in diabetic ketosis.

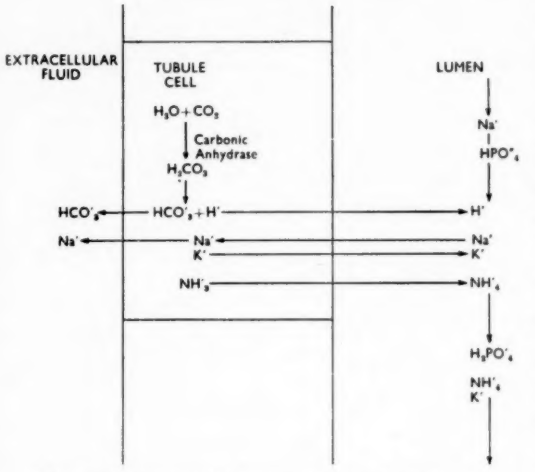

FIG. 1.—Diagrammatic representation of tubular ion exchange.

Lastly, water can be reabsorbed, independently of the solutes, under the action of the antidiuretic hormone (ADH) of the posterior pituitary (Pickford, 1956), so that the final urine volume may be varied from less than 0.5 ml. to more than 20 ml./minute according to the body's water requirements and the rate of solute excretion.

DIURESIS

Water diuresis.—When a large volume of water is drunk and absorbed, the osmotic pressure of the plasma falls and secretion of ADH ceases. As the circulating hormone is removed, distal tubular water reabsorption decreases and the volume of urine rises, its specific gravity falling, until the excess water has been excreted.

Osmotic diuresis (Bull, 1956).—An increase of unreabsorbed solute in the proximal tubule leads to an increased delivery of fluid distally, so that the final reabsorptive processes are less efficient. The volume of the urine rises and its composition more closely resembles that of glomerular filtrate; as the

flow increases the specific gravity tends to approach 1010, whatever the state of hydration of the subject. Unless sodium-retaining influences are exceptionally strong, osmotic diuresis, whatever the nature of the extra solute load, tends to remove an increased quantity of sodium as well as water. Renal function loses much of the flexibility normally imparted by selective distal tubular reabsorption; the ability of the kidney to conserve water and concentrate the urine and to excrete acid while retaining sodium is reduced.

THE DIURNAL RHYTHM

In addition to these patterns of variation in urine volume, there is in every normal subject a twenty-four-hour rhythm in the excretion of water and electrolytes, this being least during the night and greatest in the morning. This appears to reflect a rhythm of intracellular metabolism, and tends to persist when night work is substituted for daily activity. The volume of urine formed during sleep is low, owing to the reduced rate of excretion of electrolytes, whilst the specific gravity may fall soon after waking because of the osmotic diuresis produced by an increase in this rate. A change in this diurnal rhythm is often one of the earliest signs of a disturbance in one of the many influences affecting the volume and distribution of the body fluids, so that nocturia may be noticed early in the course of heart failure, Addison's disease and hepatic failure as well as renal disease.

THE ROLE OF THE KIDNEY IN HOMEOSTASIS

The kidney keeps the osmolarity of extracellular fluid (ECF) within narrow limits and so prevents the sudden changes in the water content of body cells which would follow any gross variations in the tonicity of their environment (Gamble, 1954). By independently regulating the output of sodium, it also maintains ECF volume, and it plays a part in controlling the composition of the cells by varying the rate of potassium excretion. Together with the lungs, it regulates the acid-base balance of the body. It excretes most of the end-products of metabolism and, by breaking down a large proportion of the plasma proteins every day in the process of tubular reabsorption, it may play a part in maintaining their normal composition and concentration in the blood. These are largely independent functions, although one may dominate the others sufficiently to modify them greatly.

Maintenance of ECF tonicity.—A litre of water can be drunk and excreted within four hours, with a dilution of ECF of some 2 to 5 per cent. according to the rate of absorption.

The urine flow rises to a peak, exceeding 10 ml./minute after a delay of 20 to 30 minutes, and during this time any intercellular water deficit can be made good. If this water diuresis cannot occur, as in Addison's disease, in acute renal failure or in the first 24 to 48 hours after major surgery, gross ECF dilution and water intoxication will occur. In dehydration, maximum ADH activity produces very low

volumes of highly concentrated urine; urinary sodium excretion is also greatly reduced so that water reabsorption can be further increased. There is, however, a limiting urinary concentration of about four times that of plasma, the specific gravity then being about 1040. The continued excretion of solutes maintains a corresponding minimum rate of urine flow, so that if water is not replaced the blood volume, RPF and GFR will fall and the blood urea will rise.

Maintenance of ECF volume (Wrong, 1957).—There is no doubt that the kidney retains sodium in response to a fall in ECF volume, and the site of the receptors that initiate this response, which is brought about by increased secretion of aldosterone, has been the subject of a great deal of inquiry. A fall in ECF volume also increases the secretion of ADH, and the receptors for this are probably in the wall of the left atrium, responding to a change in the degree of its filling. Disorders of these regulating mechanisms may be responsible for the œdema of heart failure, cirrhosis and nephrosis, in all of which urinary sodium may be almost completely absent. An increased intake of sodium leads to a rise in the rate of urinary sodium excretion which is much less dramatic than the response to water ingestion, and ECF volume may be expanded for a day or two before equilibrium is regained.

Regulation of acid-base balance (Robinson, 1954).—The kidney responds to acid and alkaline loads in a matter of hours and to the alkalosis of hyperventilation within minutes. To meet the need for conservation of fixed base in severe acidosis, large amounts of ammonia are formed by the tubule cells, although these may not be maximal for two or three days so that there may be large losses of sodium in the early stages of diabetic ketosis. On the other hand, an alkaline urine cannot be formed unless fixed base is excreted, sodium reabsorption being reduced and potassium largely replacing hydrogen in the ion-exchange process. The normal kidney may therefore not excrete an alkaline urine if there is salt depletion.

Potassium excretion.—The kidney conserves potassium less readily than sodium, so that the concentration in the urine may not fall below that in the plasma until there is severe depletion. In this case, hydrogen replaces potassium in the ion-exchange, so that the urine may be acid when there is a systemic alkalosis. Conversely, urinary potassium loss tends to be greater when the urine is alkaline and may therefore be considerable when carbonic anhydrase inhibitors are given.

DISORDERED RENAL FUNCTION WITHOUT RENAL DISEASE

It has long been known that all the abnormalities of uræmia could occur when the kidneys themselves were normal ('extra-renal uræmia'). Less complex disturbances of renal function may also occur from extra-renal causes (Lewis, 1957). Occasionally, one renal function may be performed so effectively that a limitation is imposed upon another. Extra-renal uræmia occurs when RPF and GFR are greatly reduced by hæmorrhage, dehydration or circulatory failure; it may be intensified by an increased rate of formation of metabolic end-products as, for instance, when blood protein is being

absorbed after gastric hæmorrhage. After major surgery and trauma there is an increased production of adrenal hormones and, for a shorter time, of ADH, which reduces water and sodium excretion while increasing that of nitrogen and potassium. In congestive heart failure and cirrhosis of the liver, sodium is retained by the kidney, probably as the result of the excessive production of aldosterone. Pituitary and adrenal deficiency reduce RPF and GFR, tubular sodium reabsorption and the diuretic response to a water load, so that the blood urea may be raised and the ECF hypotonic.

In Cushing's syndrome and in hyperaldosteronism hypokalæmia occurs from excessive urinary potassium loss, caused by adrenal hormones, and this may occur during their prolonged therapeutic administration. Hypokalæmia reduces RPF and GFR and the renal concentrating power. It often coexists with alkalosis. Hypercalcæmia also causes polyuria and, later, uræmia. Obstruction to the outflow of urine reduces GFR by opposing the filtering pressure. Occasionally, it depresses renal concentrating power to such an extent that the condition of 'water-losing nephritis' results.

In all these examples, the kidney is prevented from maintaining the normal volume and composition of the body fluids by extra-renal influences. Nearly all of them are potentially reversible, at any rate in the early stages. But prolonged renal ischæmia causes tubular necrosis, hypokalæmia appears to make the kidney liable to pyelonephritis and hypercalcæmia ultimately causes nephrocalcinosis. Early recognition of these causes of abnormal renal function is therefore important.

Occasionally, one renal function imposes a limitation upon another. In the complex disturbance that follows the prolonged vomiting due to pyloric stenosis, conservation of sodium and potassium may be so extreme that an alkaline urine cannot be formed in response to the alkalosis. A paradoxically acid urine may be formed in hypokalæmia from other causes. The excretory function of the kidney which is recovering from acute tubular necrosis may overwhelm the regulatory function with an osmotic diuresis. It is remarkable that instances of this kind should be so uncommon.

RENAL INSUFFICIENCY

Renal insufficiency may be manifest in many different ways, ranging from an isolated defect of the tubules to the total loss of all renal function in acute renal failure with anuria.

Innate functional defects of the renal tubules (Jackson and Linder, 1953; Harris, 1956).—The tubules may be unable to reabsorb water (renal diabetes insipidus), glucose (renal glycosuria), phosphate (vitamin D-resistant rickets) or amino-acids (cystinuria; Wilson's disease). The last three, sometimes with a fall of GFR and failure of acidification, occur in the Fanconi syndrome.

Acquired tubular defects are common in chronic pyelonephritis, in which varying degrees of glomerular destruction may occur with reduced GFR

and azotæmia. Loss of concentrating power is common and there may be a failure of hydrogen-ion secretion and ammonia formation (renal tubular acidosis), in which case there is loss of fixed base; osteomalacia occurs from chronic calcium loss. Occasionally the predominant tubular defect is of reabsorption of either sodium, potassium or water.

Renal failure in chronic nephritis (Platt, 1952).—As the GFR is reduced by progressive glomerular destruction, the urea clearance falls and the blood urea rises. Patients often seem to maintain a precarious balance until the former is less than 5 per cent. of normal, when irreversible derangements of body fluid composition occur. The blood levels of many substances rise with that of urea, particularly creatinine and phosphate; the rise of the latter entails hypocalcæmia which is probably a not uncommon cause of uræmic convulsions. Sodium and potassium levels are often normal until the terminal stages, but there is increasing difficulty in excreting the moderate acid load of the normal diet so that acidosis is common. In chronic renal failure, polyuria of almost fixed specific gravity and pH occurs. This is largely due to the fact that the high blood-urea level causes each remaining nephron to filter and excrete much more urea than normally, so provoking an osmotic diuresis.

Acute renal failure with oliguria or anuria leads to the retention of all the end-products of metabolism normally removed by the kidney, with loss of all regulatory function (Merrill, 1955). The levels of creatinine, urea, phosphate and potassium in the blood rise; water ingested or formed by tissue catabolism is retained together with ingested sodium, causing œdema; the abnormal accumulation of anions and failure of the excretion of hydrogen ions lead to acidosis. In the early stages of acute nephritis, severe oliguria may occur with relatively good tubular function, the urine being highly concentrated and resembling, chemically, that of prerenal uræmia.

RENAL FUNCTION TESTS

Renal function tests estimate either the rate of removal of a substance from the blood stream or the efficiency with which particular tubular functions can be performed. In the first group, the concept of *renal clearance* has been most fruitful.

The clearance of a substance is the volume of plasma containing the amount excreted in one minute. If U and P are the concentrations in urine and plasma, and V ml. of urine are formed per minute, UV mg. of the substance are excreted per minute, which is contained in $\frac{UV}{P}$ ml. of plasma. If the substance is completely removed from the plasma on its passage through the kidney, the clearance is, literally, the volume cleared per minute and must equal the RPF. It can be shown by catheterization of the renal vein that *para*-aminohippuric acid is almost completely removed in this way. The clearance of a substance excreted only by glomerular filtration, such as inulin, must equal the GFR.

Since these two clearances are reasonably constant over wide ranges of blood concentrations and urine flows in anyone not suffering from progressive

renal destruction, and since a range of normal values has been established, their estimation gives information about the presence, extent and progress of renal disease (Bradley *et al.*, 1950). But the techniques are time-consuming and are unlikely to repay the effort required except in a specialized department.

The *urea clearance*, though affected to some extent by variables such as the diet and the rate of urine flow, is sufficiently related to the GFR to give similar information more readily. Since approximately 60 per cent. of the urea filtered in the normal kidney is excreted when the urine flow is above 2 ml./minute, the urea clearance averages 75 ml./minute in a normal man, the accepted range being 64 to 99 ml./minute. (This is the 'maximum' clearance and is the blood, not the plasma, clearance since urea diffuses rapidly out of the red cells. Estimation of the 'standard' clearance, based on urine flows less than 2 ml./minute, is best avoided by adequate hydration beforehand). It is usual to collect urine for an hour, but any period can be used during which it can be assumed that the rate of urea production is steady enough to keep the level of blood urea reasonably constant, blood being drawn near the midpoint. The subject must have emptied his bladder completely at the start, and should be told to note the time on a watch when he has completely emptied it again, the average volume in ml./minute being worked out. A second period of an hour should follow on the first, any discrepancy between the two periods indicating incomplete bladder emptying. Errors due to this are larger when the volumes to be passed are smaller.

Estimation of the blood urea.—The level of the blood urea is fixed by the rate of urea production and the urea clearance; if the latter is halved while the former remains unchanged this level must double, when the rate of urea removal will again equal that of production. Changes in the blood-urea level would then give exactly the same information as do changes in the urea clearance, with the added advantage that the errors of urine collection would be avoided. In practice, the rate of urea production is affected by changes in the diet and activity, and is increased by such catabolic influences as infection and trauma, whilst the ratio of the urea clearance to the GFR may vary in renal disease. But it is roughly true to say that if a patient's blood urea rises from 20 to 40 mg./100 ml., on the same diet, then his urea clearance (and therefore his GFR) has halved. Every blood urea level between 20 and 40 mg./100 ml. is not therefore normal; this range covers a scatter of different protein intakes and ages, and the blood urea of healthy young people on an average diet is seldom above 30 mg./100 ml.

The urine concentration test.—This is best done by Fishberg's method (1954), only dry foods, without fruit, being given after midday. Urine is passed three times during the following morning; at least one specimen should have a specific gravity equal to or above 1,022. Miles *et al.* (1954) have made a valuable study of this test, pointing out that specific gravity does

not vary exactly with osmolarity; care is needed to check the instrument used. The urea concentration can be estimated in a much smaller volume of urine than that needed for the specific gravity and is therefore helpful in oliguria or after ureteric catheterization, figures even approaching the normal (more than fifty times that of blood at minimum urine flows) never being obtained in acute tubular necrosis or advanced chronic renal failure.

The urinary dilution test is of no practical value.

PSP excretion.—Phenolsulphonphthalein is excreted rapidly, mainly by the renal tubules. If 6 mg. are injected intravenously a specimen of urine passed exactly fifteen minutes later should contain more than 1.6 mg.; 3.6 mg. should be excreted in 2 hours.

This test is rapid and convenient, since the dye is easy to estimate. It is used extensively in the United States but has never found favour in this country. It may indicate a defect of tubular function even when the urea clearance is little reduced, as may occur in chronic pyelonephritis.

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ANURIA AND ITS MANAGEMENT

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Acute renal failure presenting with anuria or oliguria may result from obstruction to the renal tract, organic disease of the kidneys, or circulatory disturbances arising outside the kidney (circulatory renal insufficiency or extra-renal uræmia). The distinction between the three groups is not sharp, however, and often more than one factor is involved. Organic renal disease or obstruction may lead to circulatory insufficiency through vomiting and dehydration, or circulatory insufficiency may lead to organic renal disease through renal ischæmia. It is therefore necessary in each oliguric or anuric patient to determine the relative roles of the three main causes of renal dysfunction in producing his renal failure.

CAUSES OF ACUTE RENAL FAILURE

Obstruction to the renal tract.—Renal-tract obstruction is very easily overlooked and it is necessary to develop an automatic reaction to seek for it. When the obstruction lies in the urethra it is easy to suspect and establish but bilateral ureteric obstruction from carcinoma of the cervix or rectum must always be excluded by vaginal or rectal examination, and ureteric calculi be excluded radiographically.

Once diagnosed, the treatment of obstruction is obvious but it is often necessary to correct circulatory disturbances before the patient is fit for operation. Following relief of long-standing obstruction, it sometimes happens that the patient passes for a time into a state indistinguishable from the early diuretic phase of acute tubular necrosis. Apart from this complication and the danger of infection, which accompanies all types of acute renal failure, obstruction presents few difficulties for the physician.

Circulatory renal insufficiency.—In a wide variety of general circulatory disturbances, such as oligæmic shock from blood loss or underhydration, and in severe congestive cardiac failure, there is a marked reduction in the renal blood flow. The renal ischæmia, in turn, produces a reduction in renal function which may be severe enough to result in oliguria or anuria. This type of acute renal failure is commoner than any other and is of great practical importance, because its treatment is quite different from the other types and because lack of treatment or inadequate treatment may allow the development of organic renal damage—acute tubular necrosis. The management of such cases is the management of the underlying condition and is beyond the scope of this article, but it is as well to stress the importance of treating the condition promptly and vigorously if further complications are to be avoided.

Organic renal lesions.—Although many renal diseases may present with

oliguria or anuria, there are only three types which occur at all frequently. These are: acute tubular necrosis, acute nephritis and acute pyelonephritis; of these, the first is by far the most common. For this reason and because the principles of treatment are so alike in all types, subsequent discussion will be principally concerned with acute tubular necrosis and its management.

ACUTE TUBULAR NECROSIS

Acute tubular necrosis occurs following a wide variety of renal insults but the causes can be conveniently considered in three main groups: those due to substances toxic to the renal epithelium (e.g. mercury, phenol, carbon tetrachloride); severe renal ischæmia (e.g. the 'shock kidney', concealed accidental hæmorrhage); those of uncertain or mixed etiology in which ischæmia and toxic factors probably both play a part (e.g. crush syndrome, criminal abortion, blackwater fever, incompatible blood transfusion).

All types run the same clinical course which is described as having four phases (Bull, Joekes and Lowe, 1950):—

(1) *The onset phase*, during which the causal agent is operating. The urine volume falls to oliguric or anuric levels and the clinical picture is dominated by the primary disturbance. No histological abnormality can be demonstrated except in occasional cases by special enzyme stains.

(2) *The oliguric or anuric phase*, which may last for a period of a day or two to up to four weeks, and occasionally slightly longer. There is an almost continuous spectrum of severity but in the majority of cases this phase lasts from ten to fourteen days. During this time various disturbances of body function may occur as a result of the renal failure, and death may result. Histological changes are readily demonstrable in the tubular epithelium and rupture of the tubules may occur.

The appearance of the vessels suggests that the renal circulation is considerably slowed (Dible, 1953; Oliver, 1953) and this is confirmed by studies of renal function which demonstrate severe reduction in renal blood flow and glomerular filtration rate as well as marked disturbances of renal cell function (Bull, Joekes and Lowe, 1950).

Towards the end of this phase proliferation of surviving epithelium may be demonstrated and this coincides with a stepwise increase in urine volume which heralds the next phase.

(3) *The early diuretic phase.*—During this phase the urine volume returns to normal and often rises to very high levels of 3 or more litres a day. The hallmark of this phase is a continued deficiency of tubule function. The urine has an almost fixed composition of approximately half to one-third isotonic extracellular fluid, regardless of the state of the body fluids. The patient is in danger of water or electrolyte deficiency if his intake of these substances is lower than the rate of excretion. Alternatively, if his intake is greater than the rate of urinary loss, he may become overhydrated or develop electrolyte poisoning. Studies of renal function and the histological changes are again consistent with the disorders found. This phase usually

lasts for as many days as the preceding period of oliguria or anuria, but very occasional cases have been described in which the oliguric phase has been short-lived or absent (Teschan *et al.*, 1955; Sevitt, 1956).

(4) *The late diuretic or recovery phase* follows, in which tubule function returns and the histological picture returns to normal apart from an occasional scar.

CAUSES OF DEATH IN ACUTE RENAL FAILURE

Analysis of the causes of death in acute renal failure is difficult because, so often, the primary condition causing the failure is itself potentially lethal. This is well illustrated by the fact that mortality figures of over 90 per cent. have been quoted in tubular necrosis following battle injuries (Lucké, 1946), whereas I have not lost a single patient with anuria following concealed accidental hæmorrhage in the last twenty patients treated. Furthermore, the mortality and symptomatology in acute renal failure are greatly altered by the treatment given. Whereas ten years ago most patients died a uræmic death, usually due to overhydration or electrolyte imbalance, nowadays the most important cause of death is infection. The third most important cause of death is hæmorrhage, but this is uncommon.

Uræmic deaths are mainly due to disturbances of water and electrolyte balance. They may occur in the oliguric or early diuretic phase and may be due either to retention of water and electrolytes or to uncontrolled loss of these substances. Simple overhydration of either the cellular or extracellular compartments or of both is the most common disturbance. When the cellular compartment alone is affected, nausea, vomiting, stupor, confusion, muscular twitchings and epileptiform convulsions may occur. This water intoxication may present during the oliguric period as a result of too high a fluid intake or during the early diuretic phase as a result of sodium chloride loss. In either case one finds a lowered serum-sodium concentration and a lowered mean corpuscular hæmoglobin concentration; the latter is an indication of the cellular dilution.

When extracellular overhydration is more prominent, this is usually due to excessive salt intake as well as too high a fluid intake. The picture is one of peripheral œdema, and signs of congestive cardiac failure are present. This form of 'cardiac' failure is peculiarly resistant to digitalis and death occurs with pulmonary œdema.

Cellular underhydration occurs in some cases, especially in the early diuretic phase, and is usually due to an excessive intake of salt combined with water loss. If the patient is conscious he complains of thirst. Later he becomes stuporose or comatose and often develops coarse twitchings rather like those seen in hepatic coma. Particularly in children, pyrexia may occur —sometimes as high as 103°F. (39.5°C.). The tongue is wrinkled and in some cases the muscles have a 'doughy' feel. The plasma sodium concentration is high.

Extracellular underhydration may occur in the early diuretic phase and presents the usual picture of oligæmia. The plasma-protein concentration and plasma specific gravity are high.

Potassium intoxication with death from cardiac arrest sometimes occurs, especially in the oliguric phase, usually due to catabolic processes releasing potassium from the cells. It occurs particularly in the crush syndrome, following war wounds and in the presence of infection. Potassium deficiency may occur in the early diuretic phase due to an uncontrolled loss of the ion at that time. It presents with a flaccid, areflexic paralysis and both hyperpotassæmia and hypopotassæmia may be recognized by blood analysis or electrocardiography (Merrill, 1955). A tendency to acidæmia is common in both the oliguric and early diuretic phases and presents with the usual picture of hyperventilation and lowering of the level of consciousness. Other ionic disturbances involving calcium and magnesium may occur occasionally.

In addition to uræmic symptoms attributable to ionic disturbances and water imbalance, there are other uræmic syndromes whose mechanisms are not clear. Stupor, twitching, coma and convulsions may occur even when there is no abnormality of water or electrolyte balance. These are probably due to retention of various organic radicals. Stomatitis, gastritis and colitis are not infrequent and may be severe. They may be due to urea-splitting organisms causing local high concentrations of ammonia. Pericarditis and pleurisy may occur and the mechanism is unknown. Anæmia may develop and is sometimes hæmolytic but also has a dyshæmopoietic element.

Infection.—Gross disturbances of water and electrolyte balance are uncommon nowadays because of a general awareness of their importance but infection remains a serious problem. By far the commonest type of infection is broncho-pneumonia and the commonest infecting organism the staphylococcus, which is usually penicillin resistant. Cystitis and pyelitis are common and occasionally severe. To a large extent this must be attributed to the use of that pernicious instrument, the catheter. Other infections of muscle, in war wounds and the crush syndrome, and peritoneum and pelvic organs in abortion cases, also occur.

Hæmorrhage is an uncommon cause of death and occurs particularly in the severely infected case.

PRINCIPLES OF TREATMENT

When oliguria or anuria is due to a removable cause such as obstruction or circulatory renal insufficiency, the treatment is obvious. Similarly, in some cases in which a true renal lesion underlies the renal failure appropriate steps may be taken to remove the cause. For example, pyelonephritis may be treated with appropriate antibiotics, or cortisone be administered in the visceral angiitides. Prophylactic measures may be taken, such as prompt treatment of shock or other circulatory insufficiency, or in cases of poisoning a suitable antidote may be administered (e.g. dimercaprol in mercury

poisoning). For the rest, management must be directed towards the avoidance of infection and the maintenance of a normal water and electrolyte balance for sufficiently long to allow repair processes in the kidney to occur.

Anti-infective measures.—It is now generally agreed that these patients should be isolated and in particular protected from the inhalation of organisms from the atmosphere and from attendants. A form of barrier-nursing, with all attendants masked and gowned, should be used and the patient's bedding should be sterilized by means of quaternary ammonium compounds or by stoving. During bed-making and ward-cleaning the patient should wear a mask. To promote adequate breathing, the patient should be encouraged to move about in bed and even sit in a chair.

Opinions differ as to the advisability of administering antibiotics routinely, but my practice is to give 1 mega unit of penicillin by injection on admission and 0.25 mega unit a day thereafter as a single injection. Larger doses often give rise to rashes after about ten days because the material is retained and very high blood levels are achieved. Other antibiotics should not be given as a routine but should be reserved for administration if infection supervenes. In the case of all antibiotics other than penicillin the dosage must be carefully adjusted because they are excreted by the kidney and toxic levels may develop. This is particularly important in the case of streptomycin. For example, I recommend a loading dose of 1 g. of streptomycin, or of the tetracyclines, followed by 0.25 g. daily until a total dosage of 2 g. has been given.

Catheterization should be avoided at all costs except when trauma to the urethra or bladder demands it. Infection invariably follows even a single catheterization in an anuric subject.

Maintenance of water and electrolyte balance.—It is important to appreciate that the majority of the uræmic states result from an imbalance between the rates of intake and production of water and chemical substances and their rates of excretion by all routes. Normally the kidney adjusts the rate of excretion of water and most electrolytes and many organic substances so as to maintain normal quantities in the body. In renal failure in general and in oliguric and anuric states in particular this function is lost and it is the physician's duty to ensure that balance is maintained by other means, particularly by adjustment of the intake or rate of production in the body or, in certain circumstances, by providing an alternative route of loss to the kidney.

Water balance is the resultant of the intake and rate of production of water from body metabolism on the one hand and the insensible loss in the breath, through the skin and in fæces, plus urine loss and loss in vomitus or diarrhœa on the other. Insensible water loss in the apyrexial subject amounts to approximately 700 ml. in our climate but simple replacement of this quantity in the diet results in overhydration because, as Hamburger and Mathé (1954) and others have shown, considerable quantities of water are

produced from body fat as well as from metabolism of any food given. For this reason the basic fluid intake should lie normally between 400 and 600 ml. a day. When urine is being passed, or fluid loss through other channels is occurring, a volume of water equal to this must be added to the basic intake.

Exceptions to this rule are as follows:—

(a) If one is fortunate enough to see a patient in the onset phase during, for example, a hæmolytic transfusion accident or immediately after poisoning with a nephrotic agent, 1 litre of 50 per cent. glucose should be administered immediately as rapidly as possible in the hope of inducing an osmotic diuresis which, at least in experimental animals, has been shown to prevent or diminish tubule damage.

(b) If the patient is anæmic, blood should be administered but the volume of blood can be neglected in calculating the daily water balance.

Electrolyte balance.—In an anuric subject it is clear that no electrolyte should be administered except to correct deficiencies which are leading to circulatory renal insufficiency. A mineral-free diet, however, does not prevent accumulation of potassium in the extracellular fluid. It is derived from the cells and released during the process of catabolism. In order to minimize this potassium release the patients should be given a protein-sparing diet, usually in the form of carbohydrate, and anabolic hormones such as testosterone or one of the newer non-virilizing androgens should be administered.

During the early diuretic phase there is an uncontrolled loss of sodium, chloride, bicarbonate, potassium and magnesium and these must be quantitatively replaced. In most cases of moderate severity (say up to 12 days' anuria) daily analysis of the urine for these ions is unnecessary. Replacement can be calculated on the assumptions that the urine contains approximately 70 mEq. Na and 50 mEq. of Cl per litre and that the daily potassium loss is approximately 1 to 2 g.

PRACTICAL CONSIDERATIONS IN TREATMENT

These considerations can be put into practice by means of the following instructions to ward staff:—

(1) Exclude and treat if necessary any obstruction or circulatory insufficiency.

(2) The patient should be barrier nursed.

(3) Avoid catheterization.

(4) Keep intake and output charts.

(5) Administer 1 mega unit of crystalline penicillin by single intramuscular injection on admission and 0.25 mega unit daily thereafter.

(6) Administer 50 mg. of testosterone as isobutyrate crystals ('perandren') by a single intramuscular dose.

(7) *Diet in the oliguric phase.*—During the oliguric phase and for the first

two days after the urine flow exceeds 1 litre a day give a basic intake of 500 ml. of 50 per cent. glucose, to which are added further volumes of fluid as indicated on p. 269. If the patient is not vomiting or only vomiting small quantities, this may be given by a slow intragastric drip spread evenly through the twenty-four hours.

A 1- to 1.5-mm. bore polythene tube is preferable to rubber tubing because it is slightly more rigid and difficult to vomit out. It should be passed through the nose until the lower end has just entered the stomach. If a greater length is passed it may fatigue due to movement in the stomach and fracture. While the tube is being advanced its position should be checked by injecting air through the tubing while listening over the epigastrium with a stethoscope. As soon as bubbling is heard the tube should be stopped and attached to the facial skin by adhesive plaster.

If vomiting occurs the vomitus should be collected, filtered through lint and replaced by adding to the remaining 50 per cent. glucose. This avoids complicated analyses of the vomitus and, provided the patient is not informed of what is happening, causes no offence. If vomiting becomes so severe as to make replacement difficult, or if the patient develops marked diarrhœa, the 50 per cent. glucose may be administered intravenously. In this case it is important to pass an intravenous catheter—usually of polythene, 1- to 1.5-mm. bore—into a large vein such as the superior or inferior vena cava. I prefer the former. The actual procedure for passing the tubing is as follows:—

The tip of the polythene is smoothed by rubbing on cloth and the tubing sterilized in a quaternary ammonium compound or by formalin vapour. The patient should be propped in bed, sitting at an angle of 45° and his head positioned with the occiput resting on the shoulder of the side through which the tubing is to be passed. After washing both outside and inside with isotonic saline or 5 per cent. glucose solution the tube is passed via the antecubital vein until 10 to 12 inches (25 to 30 cm.) have entered the venous system. Blood should now flow back easily on gentle suction with a syringe. The blood should now be ejected and the tubing filled with isotonic saline or 5 per cent. glucose and the syringe detached while the outer end of the tubing is held up. The column of saline or glucose will fall and can be observed through the transparent tubing which is now used as a manometer. Modest pulsation should be visible and the mean pressure should lie at about 5 to 7 cm. below the sternal angle with an inspiratory downswing and expiratory upswing. To exclude the tip's having passed up the jugular vein the neck should be compressed and if this causes a rise in pressure in the tubing it must be reinserted. If there is a paradoxical swing in pressure with respiration, the tip is in the inferior vena cava or liver and must be withdrawn a few inches. If the pressure is higher than that indicated and if pulsation is marked, the tip is in the ventricle and must be withdrawn. Finally, a syringe full of blood must be withdrawn. If it is very dark the tip may be in the coronary sinus—a very dangerous position—and must be withdrawn a few inches. This very rarely happens.

Once these checks have been made the tubing may be connected to an ordinary drip-set containing the quantity of 5 per cent. glucose and the drip be set at a very slow rate so as to last evenly throughout the twenty-four hours. Five hundred units of heparin may be added to the bottle of glucose to prevent clotting at the catheter tip. The central venous pressure may be observed once or twice a day as above and the tubing may also be used to obtain blood samples as indicated.

The following additions to this basic intake should be made:—

The volume of any vomitus which has not been returned by the intragastric tube should be measured and to this be added the volume of urine and the volume of

any diarrhœa or other measurable fluid loss. This total volume should then be replaced by an equal quantity of the following mixture by intragastric drip:—

Sodium bicarbonate	1 g.
Sodium chloride	3 g.
Glucose	100 g.
Water	to 1 litre

When the intragastric route is not feasible, the following mixture may be given intravenously through the polythene tubing:—

1/6 molar sodium-lactate solution	150 ml.
Isotonic saline solution	350 ml.
5 per cent. glucose solution	500 ml.

for each litre of measurable loss.

(8) *Diet during the early diuretic phase.*—Two days after the urine volume exceeds 1 litre in twenty-four hours the feeding by intragastric or intravenous tube may be stopped and the patient placed on a diet consisting of the following:—

Fruit juice, tea, coffee, and water of a volume equal to the measured losses plus 500 ml.

Toast, jam, boiled sweets and fruit may be given liberally, but if juicy fruits such as oranges are used the fluid intake must be decreased accordingly.

To this diet must be added 1 g. daily of potassium chloride and 1 g. of sodium bicarbonate and 3 g. of sodium chloride per litre of measured fluid loss.

This regime should be maintained for as many days as the patient has been oliguric or until the blood urea has fallen below 100 mg. per 100 ml., whichever is the shorter.

(9) *Blood samples.*—The blood should be analysed on the seventh day of anuria or oliguria, or earlier if uræmic symptoms become evident. The following determinations are useful: plasma specific gravity, sodium, potassium, carbon dioxide combining power and urea. Thereafter samples should be taken at three-day intervals for the same analyses or more often in the presence of symptoms.

PROGNOSIS AND MANAGEMENT OF COMPLICATIONS

The conservative regime outlined is usually satisfactory in patients who are seen early in the course of tubular necrosis and in whom there is no very serious associated condition. Such patients should nearly all recover. Minimal disturbances of renal function persist, but can only be demonstrated by special techniques. Even in their presence further pregnancies may be permitted.

In patients with severe injury, severe infection and marked disturbances of water and electrolyte balance, the prognosis is extremely grave. In such cases the basic regime must be modified in various ways according to the complications found. Practical measures for dealing with disturbances in water and electrolyte balance and other complications are described elsewhere (Bull, 1955). The following additional point, however, requires mention.

Herndon (1957) has shown that in patients with a tendency to hyper-

potassæmia, anoxia may raise the serum potassium dramatically in the space of less than a minute. It is therefore vital to maintain an adequate airway and ample pulmonary ventilation in such patients.

THE ARTIFICIAL KIDNEY

Certain patients are unlikely to survive by the use of conservative measures alone, and various dialysis procedures may then be used. Of these, there is now little doubt that the artificial kidney in one of its forms is to be preferred to peritoneal dialysis, intestinal dialysis or exchange blood transfusion. Improvements in the instrument and in the technique have made it a safe procedure in the hands of those teams with sufficient experience of its use. In my opinion, however, its main value has been that of a neon sign directing to certain centres material which has given the operators a large experience of treating anuric patients. The proportion of patients saved by the machine is still probably small, and I would estimate that a civilian population of between 5 and 10 million is the minimum which would warrant the installation of an artificial kidney. The indications for its use are still far from clear, but I would recommend the early transfer to an artificial kidney unit of any anuric or severely oliguric patient with severe muscle injury or infection which will not rapidly respond to appropriate antibiotics. Hyperpotassæmia is not, to my mind, an indication for dialysis, unless it is associated with severe injury or infection, or occurs in patients in whom ion-exchange resins cannot be used. Patients with anuria or severe oliguria of more than fourteen days' duration should probably be transferred to an artificial kidney unit and anuric or oliguric patients who have received more than 3 g. of streptomycin may also require dialysis.

SUMMARY

The causes of acute renal failure are considered and, as an illustration of the principles of treatment, the management of acute tubular necrosis is described in some detail.

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NEPHROSIS AND ITS MANAGEMENT

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THE gross œdema which proclaims the onset of the nephrotic syndrome is obvious and alarming to patient and physician alike. The extreme degree of albuminuria which provokes this œdema may be a symptom of many rare conditions (e.g. renal vein thrombosis, amyloidosis, polyarteritis nodosa, anaphylactoid purpura, drug reaction, diabetic nephropathy), but for practical purposes the vast majority of cases belong to one of two patterns which may be described as 'nephrosis' and 'nephrotic nephritis' respectively.

NEPHROSIS

Etiology.—The causes of nephrosis are not clearly defined but almost certainly multiple factors are concerned. Alterations in the serum complement make it likely that an abnormal antigen/antibody response is present in some cases; a high incidence of nephrosis in babies aged about one year has suggested mercury in teething powders as another factor. In the great majority of cases occurring during childhood there is no history or evidence to suggest preceding acute hæmorrhagic nephritis. The basic lesion is damage to the nephron resulting in the leakage of plasma albumin into the urine. The full facts concerning the histopathology involved remain obscure.

Clinical picture.—The illness has its highest incidence during the second year of life, is uncommon in children aged more than seven years and is rare in adults. There are usually no premonitory symptoms or signs such as a sore throat, or acute tonsillitis. An apparently healthy toddler is noted to have 'puffy eyes' (periorbital œdema) and alarmed parents seek medical advice. Pitting œdema of the ankles and lumbar region is usually detectable and is often accompanied by ascites. The blood pressure is not raised. On boiling the acidulated urine, a very heavy cloud of albumin is detected and alternative tests for albuminuria such as the salicylsulphonic acid test are strongly positive. The patient has oliguria and a few casts may be present in the urine but urea is normally concentrated. Occasional red cells may be seen in the urine but no gross hæmaturia exists. The biochemical features of the plasma at this stage are a very low albumin level, a normal level of urea, and a high cholesterol level. The erythrocyte sedimentation rate is markedly accelerated.

Course.—The œdema of these patients may last for days, weeks, months or years. It may become gross, so that the eyelids cannot be opened, the umbilicus is everted, and the scrotum distended with fluid. Ascites tends to displace the liver so that dullness on percussion is noted over the base of the right lung; hydrothorax may occur. The degree of œdema fluctuates

widely and its distribution is affected by gravity. These œdematous patients have low plasma gamma-globulin levels and are peculiarly vulnerable to infection, often pneumococcal in type. Before the introduction of antibiotic therapy such infections often proved fatal; in other instances they were followed by temporary diuresis and, on rare occasions, led to recovery.

In most cases the œdema eventually decreases but when spontaneous recovery does not occur heavy albuminuria may persist for years. Such patients are often asymptomatic but episodes of œdema may occur from time to time and wasting may be evident. If renal function remains efficient the patient can survive for twenty years or more. In the terminal phase progressive renal failure sets in, urea clearance becomes inadequate and metabolic end-products accumulate. As a result, progressive uræmia with acidosis and air hunger ensues. Coma then supervenes and death inevitably follows.

Prognosis.—The outlook in children is fairly good. Œdema is readily removed by modern therapy and at least 50 per cent. of patients make a spontaneous recovery as judged by the disappearance of albuminuria, the last sign to disappear. They continue in this asymptomatic state for many years and may be presumed healthy after ten years free of albuminuria. The principal danger lies in infection during the early œdematous stage and most deaths within two years of the onset are due to this. The prognosis is particularly good in very young children in whom œdema is often short-lived. Mortality in the early stages is higher in boys than in girls, but girls are more likely to have persisting albuminuria.

NEPHROTIC NEPHRITIS

At the outset of the illness most adult patients and a few children have definite evidence of glomerulitis and impaired renal function. They may have all or some of the following:—hypertension, gross hæmaturia, cellular casts in the urine, poor urea concentrating power and a high blood urea. In addition the characteristic albuminuria, œdema, hypoproteinæmia and hypercholesterolæmia of nephrosis are present.

Course.—Macroscopic hæmaturia, hypertension and urea retention usually diminish after a few days or weeks but the gross albuminuria and œdema persist, often with microscopic hæmaturia. It is at this stage (i.e. some weeks after the onset, when hæmaturia and hypertension have abated) that this condition most closely resembles nephrosis as already described. Patients are often not seen at hospital until this stage has been reached. The œdema and albuminuria of nephrotic nephritis are less labile and more difficult to eradicate. Such patients seem less vulnerable to infection than the child with nephrosis.

Prognosis.—The outlook in nephrotic nephritis is very poor. Œdema tends to recur intermittently, albuminuria persists, and renal failure eventually occurs. Such patients usually die within ten years of the onset and less than 20 per cent. regain good health and freedom from albuminuria. Since most

adult nephrotics are of this type it follows that the prognosis of the nephrotic syndrome in adults is bad.

Although in many instances 'nephrotic nephritis' may be readily differentiated clinically from 'nephrosis' the two conditions merge imperceptibly. To avoid useless controversy one usually speaks of the nephrotic syndrome to include all cases, with the mental reservation that hæmaturia and other signs of glomerular damage at the onset materially alter the probable course of the illness.

GENERAL MANAGEMENT

During the period of gross œdema and ascites the patient is lethargic, bloated and content to rest in bed. Treatment during this stage is aimed primarily at eliminating œdema and albuminuria by the use of dietetic and steroid therapy. If the scrotum becomes grossly distended it should be supported and the foot of the bed considerably raised to promote drainage. Very exceptionally, gross ascites causing distressed respiration may require paracentesis but nowadays this should not be necessary except when medical relief of ascites would take too long. Southey's tubes should never be needed today. When gross periorbital œdema exists the head should be raised and the eyelids will drain by gravity.

There is little evidence that rest in bed itself improves the condition and as the length of the illness increases and the œdema lessens he should be allowed to get up and about. With varied activity and a more liberal diet many patients with continuing albuminuria can lead a happy and active existence for a number of years. Since steroid therapy became available many more patients have been rendered free of œdema but not of albuminuria and it seems likely that the non-œdematous stage of nephrosis will become more prominent in the future.

When renal failure finally ensues the hypertension and uræmia probably will not distress the patient but the concomitant anæmia may do so. No medication is likely to cure this anæmia but blood transfusion effects temporary improvement. The retention of acid metabolic products may be countered to some extent by alkalis such as calcium lactate, sodium citrate, or sodium bicarbonate in dosage of about 60 grains (4 g.) six-hourly. Unfortunately, as renal failure proceeds the plasma calcium level becomes lower and alkali treatment may initiate or aggravate tetany. This painful spasm of wrists and ankles may be relieved temporarily by the intravenous injection of 10 ml. of 10 per cent. calcium gluconate. Sedation may be required in the stage of mental confusion preceding terminal coma.

DIETETIC MANAGEMENT

If evidence of glomerular damage such as hæmaturia and hypertension is present at the outset, it is wise to moderate the intake of protein, sodium and fluids. A diet consisting of 1 pint (570 ml.) of milk, together with glucose drinks amounting to another pint daily, is easy to measure and to take. This

restricted intake should be limited to the initial period of illness and the diet increased as soon as kidney function improves and the hæmaturia decreases. During the stage of œdema two factors of importance are the excessive sodium retention (leading to œdema and oliguria) and the gross protein loss in the urine. Efforts are made to slow up œdema formation or promote diuresis with a diet low in sodium. This is achieved by cooking vegetables without salt, adding no salt to the food and reducing the intake of milk to one pint (570 ml.) and of bread to six thin slices daily. Salty foods such as smoked fish, tinned meat and soups should be avoided. This diet amounts to about 2 g. of sodium daily and is given throughout the period of steroid therapy. 'Neoselarom', a sodium-free salt substitute, may help the palatability of the diet. Since the function of the kidney in removing urea is usually adequate the diet should not be restricted in protein content. When sodium retention decreases the œdema lessens but albuminuria usually continues. The patient should receive a diet of high protein content so long as urea clearance remains adequate. This is achieved by giving 1 to 2 pints (570 to 1100 ml.) of milk and large portions of cheese, meat, fish, potatoes and pulses. If sodium retention persists then less milk and bread low in sodium should be given. This diet is palatable and the high protein intake compensates for the continuing drain of protein in the urine, thereby sparing endogenous tissue protein and lessening emaciation.

This stage of the illness may last for many years but eventually, with the onset of renal failure, the blood urea begins to rise. It then becomes important to give a copious intake of water since urea concentration will by now be very poor. The patient is literally drinking for his life, or at least to keep his blood urea level within limits compatible with survival. Since a diet high in protein will add to the likelihood of uræmia less protein should be allowed, always remembering that at this stage all treatment is palliative, and that rigorous dietetic restriction may irk the patient and not delay his death.

STEROID TREATMENT

Since 1950 a new group of hormones and allied steroids have outmoded and displaced the many ineffective treatments previously in vogue. In this country oral cortisone rapidly found favour whilst in the United States intramuscular corticotrophin was popular with physicians. Their enthusiasm for injections was probably not shared by their patients! Both these hormones had two serious drawbacks in that they caused sodium retention (thereby aggravating the œdema) and that the results obtained with them were highly unpredictable.

In 1956 prednisolone became firmly established as the treatment of choice. This synthetic steroid is four to five times as powerful a glucocorticoid as cortisone but has much less sodium-retaining activity. Before starting prednisolone therapy one should treat any infection which is detected. Neither moderate hypertension nor nitrogen retention is a contra-

indication to treatment, but both these points should be carefully monitored. If hæmaturia is present at the onset one usually waits for it to ameliorate before starting treatment. The dosage schedule advised is as follows, irrespective of the age or size of the patient:—

Days 1-10: 20 mg. prednisolone 8-hourly = 60 mg./day
11-20: 20 mg. prednisolone 12-hourly = 40 mg./day
20+ : 10 mg. prednisolone 12-hourly = 20 mg./day

The dosage of 20 mg. a day is then slowly reduced over a prolonged period, provided the albuminuria continues to decrease. Any sign of a gross increase

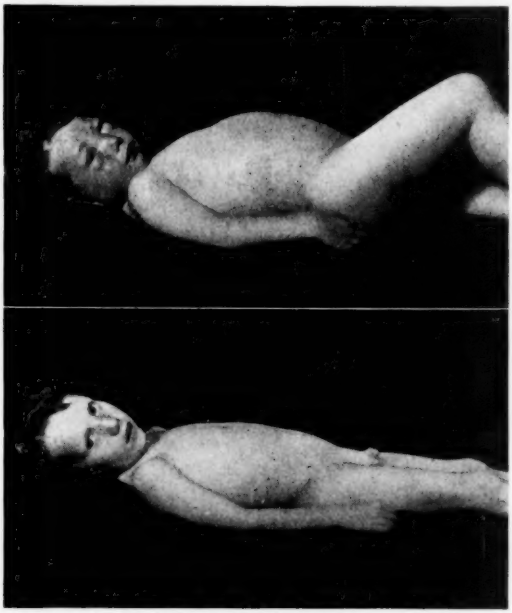

FIG. 1.—Two photographs of a child with nephrosis: (a) before steroid therapy; (b) three weeks later. Note how the rounded contours of œdema mask underlying wasting.

in albuminuria is an indication to increase dosage, but it should be remembered that the concentration of protein in the urine will vary with the volume of urinary output. The patient may be retained on maintenance dosage of 10 to 15 mg. of prednisolone daily for many weeks or months. It is our practice to give 10 mg. of corticotrophin gel intramuscularly daily for the last week of prednisolone treatment, in order to stimulate the adrenal glands of the patient. Throughout hormone therapy the patient should receive a diet containing less than 2 g. of sodium daily as described above.

Results of steroid therapy.—Diuresis occurs in the majority of children with nephrosis within three weeks of starting prednisolone treatment and both

œdema and ascites usually clear completely. The rounded contours of the œdematous patient mask underlying wasting which is revealed by the sudden loss of fluid. This loss may amount to 50 per cent. of the patient's final weight. Figure 1 shows a child before and after diuresis and illustrates these points. More significant is the fact that the total amount of protein lost in the urine daily markedly decreases at approximately the same time as diuresis occurs. This happening is shown in figure 2. The decrease of proteinuria following steroid therapy may be temporary or permanent. Treatment today resolves into a question of continuing prednisolone in dosage adequate to suppress albuminuria for as long as is required.

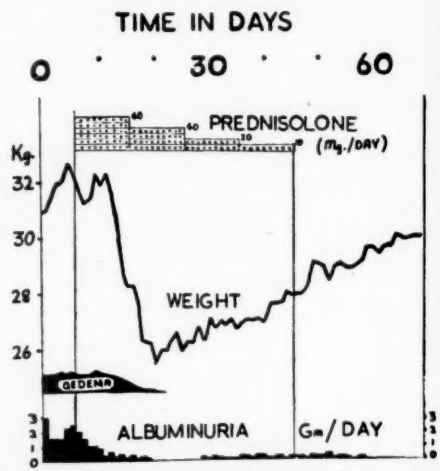

FIG. 2.—Chart illustrating the effect of prednisolone treatment on the weight, albuminuria and œdema of an œdematous nephrotic patient. The precipitous fall in weight is due to diuresis and loss of œdema; the ensuing steady gain follows amelioration of albuminuria and is not due to returning œdema.

Following the rapid loss in weight due to shedding œdema and provided the albuminuria decreases to minimal amounts, the patient rapidly gains weight. This steady increase is due to the laying down of muscle and fat and should not be confused with a return of œdema (fig. 2).

Side-effects of steroid therapy.—Practically all patients thus treated show deposition of fat and the development of a 'moon-face'. This can be limited to some extent by maintaining the calorie intake at a level approximating to that obtaining before treatment. Striæ resembling those of Cushing's syndrome may develop in adults. Fæcal impaction is not uncommon and may be mistaken for acute intestinal obstruction by the unwary but is soon remedied by enemas. Hæmatemesis and ulcer formation are rare in children but not uncommon in adults. A moderate amount of glycosuria may occur but is seldom significant.

One important point must be mentioned: during rapid diuresis the plasma potassium level may fall rapidly and convulsions may occur. Potassium chloride, 1 gramme six-hourly, should therefore be given during such rapid diuresis to prevent hypokalæmia, and repeated estimations of plasma potassium levels are advisable. Hypertension may appear or increase during steroid treatment but prednisolone seems safer in this respect than prednisone.

Failure of steroid therapy.—In a number of cases, particularly in adults

and when hypertension and hæmaturia are present in the early stages, treatment with steroids may fail. Sometimes a second course may succeed but, if œdema and ascites persist despite adequate steroid therapy, chlorothiazide may be tried. The initial dosage should be 500 mg. twice daily and this should be increased progressively by 500 mg. twice daily to as high as 2 g. twice daily if no diuresis occurs. It is imperative that repeated estimations of plasma potassium be carried out when such treatment is given, since large amounts of oral potassium chloride may be needed to prevent hypokalæmia. Chlorothiazide is usually successful in clearing the ascites and the œdema from chronic cases, and a low-sodium diet should be given during such treatment. The underlying albuminuria persists, and maintenance dosage of 500 mg. of chlorothiazide twice daily may be required to keep the patient free of œdema.

Management of infection.—If infection arises during treatment it should be treated with antibiotics since steroid therapy may interfere with the patient's antibody response. Since many infections are pneumococcal or streptococcal in origin, penicillin is usually effective. In this country, we have not found antibiotic prophylaxis necessary as a routine measure during steroid therapy. On the other hand, when respiratory infections precede relapses, sulphadiazine, 0.5 g. twice daily for a period of years, may benefit the patient.

DISCUSSION OF RESULTS

Recent advances in treatment have been so rapid that it behoves us to pause and consider to what extent the outlook in nephrosis has been altered. The most striking improvement is the decrease in the number of deaths during the first few years after onset. This mortality was almost entirely due to infection and superficially it would seem that credit must go to antibiotic therapy. This, however, is not by any means the whole answer. Sulphonamides and penicillin have been used here since 1938 and 1944 respectively and are effective against both pneumococci and streptococci yet the fall in early mortality has been more marked in the past six years. It seems that other factors are at work. One of these is almost certainly the reduction in the duration of œdema brought about by steroid therapy. The patient freed of œdema is less liable to infection; this applies especially to œdematous infants in whom diarrhœa often proved fatal. Furthermore, with steroid therapy the plasma gamma-globulin content rises to within normal limits from the low levels initially obtaining. This rise may be related to the patient's ability to withstand infection.

Has steroid therapy altered the eventual outcome of nephrosis? This is a question which time alone will answer. The outlook in nephrosis in children has always been fairly good. One would anticipate that more than 60 per cent. of such cases are now likely to recover completely, and a further 25 per cent. will continue with albuminuria for a period of many years to come. Such improvement can be explained as due to the elimination of deaths

from infection in the early stages enabling more patients to make a natural recovery. Steroid therapy has a decided effect in removing œdema and reducing albuminuria but probably conceals rather than eliminates the underlying disease process. It should be continued over a long period as a form of protective treatment.

With definite evidence of glomerular involvement present the outlook is very different. Not only are the œdema and albuminuria of these patients difficult to eliminate with steroid therapy, but the hæmaturia, nitrogen retention and hypertension may persist and renal failure is the usual termination. When steroid therapy is ineffective chlorothiazide is of value in controlling the œdema but does not usually reduce the albuminuria. Its use is fraught with the danger of hypokalæmia. Since successful treatment with steroids removes the œdema and albuminuria it is not necessary to give prednisolone and chlorothiazide together. The combination of these two may cause grave electrolyte imbalance.

Triamcinolone is a new steroid widely advertised at present. The use of this hormone in nephrosis is based on flimsy published evidence. Results obtained here so far have been inferior to those obtained with prednisolone and it seems undesirable to treat nephrosis with triamcinolone until adequate experience of a larger number of cases is published.

Many other forms of treatment have been tried recently including artificially produced infections (such as malaria), cation-exchange resins and carbonic anhydrase inhibitors. Any of these may occasionally benefit a patient, but they rarely produce recovery, are potentially dangerous and should only be tried in the last resort. Mercurial diuretics may aggravate the renal damage and cause the death of the patient; their use nowadays is contraindicated.

SUMMARY

During the past fifteen years the clinician has been given three new and powerful types of treatment with which to combat the nephrotic syndrome. These are the antibiotics, the steroid hormones, and chlorothiazide. By the judicious use of these to overcome infection and to reduce albuminuria and œdema, together with prudent dietetic management, the lot of the patient with nephrosis has been greatly improved. The reduction in the duration of œdema, achieved without turning the patient into a veritable pincushion, is a distinct step forward and one is encouraged to hope that the eventual prognosis has been materially improved.

THE MANAGEMENT OF GENITO-URINARY TUBERCULOSIS

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The area served by the hospital concerned in the work of this survey is that of a little over five counties of the south-eastern area of Scotland. These are largely rural, with small manufacturing or mining towns and some fishing villages. The total population of the area is about 200,000 but many patients have been admitted from the city of Edinburgh. The proportion of cases of genito-urinary tuberculosis transferred to our care from Edinburgh was probably not very high.

SOME GENERAL CONSIDERATIONS

Borthwick (1956) has pointed out that in the west of Scotland there is a marked fall in the number of patients with pulmonary tuberculosis who require admission to hospital; this has not been accompanied by a comparable fall in the number who have suffered from genito-urinary tuberculosis. He and others (e.g. Gloor, 1946; Wallgren, 1948) have suggested that from a clinical viewpoint tuberculosis of the genito-urinary tract was usually the last of the various visceral manifestations of the disease and that a period of from eight to ten years might elapse between the supposed time of the infection of the kidney and the initial clinical symptoms. In 1950, we admitted 160 patients suffering from pulmonary tuberculosis and four patients suffering from genito-urinary tuberculosis. In 1957, subsequent to mass radiography, the comparable numbers were respectively 279 and seven. In rural and semi-urban areas the number of cases of genito-urinary disease should be low, but there will always be a limited number who will develop the disease after a fairly lengthy latent period, or long after the original infection.

The existence of renal tuberculosis is often proved by examination of the urine or urinary systems of patients who may feel and look comparatively well. Those with genital tuberculosis usually exhibit few signs of toxicity or general illness. At first sight therefore it may not seem appropriate that such patients should be formally notified as cases of tuberculosis, and, still less, that they should be admitted to a special hospital. In our view, however, both are of the utmost value. Notification will ensure the examination of the family and other contacts in a circle where a tuberculous infection has existed and may persist, and it also sets in motion the machinery for the social care and rehabilitation of the individual patient and perhaps of his family.

We are convinced that at present the larger tuberculosis hospitals which possess clinical, laboratory and, preferably, operating-theatre facilities, offer the most suitable environment for such patients. Obviously those with combined pulmonary and urogenital lesions will be admitted to such hospitals, but it is our experience that even those in whom no lesion can be demonstrated in systems other than the urogenital have accepted a regime of rest in hospital, chemotherapy, operation if necessary, and very prolonged after-care without difficulty, and with clinical results which, we feel, have fully justified this policy.

To achieve such results there must obviously be a close liaison between the physician and surgeon, who can together benefit from experience of the efficacy of various forms and durations of chemotherapy and of surgical procedures in necessary cases, and at the most suitable time.

In 1950, when a scheme of admission of patients with genito-urinary tuberculosis was begun with full cooperation between the tuberculosis physician and the urological surgeon, there was an average of 10 to 12 such patients in the hospital at any given time. That this figure has now dropped to 2 to 4 patients is due in part to the availability of beds in a city hospital within easy reach of the homes of a proportion of patients, and a marked falling-off in the number referred with a diagnosis of genito-urinary tuberculosis.

PRINCIPLES OF THERAPY

The chemotherapy of tuberculosis has altered in detail since its inception mainly in the combinations of the three main drugs and in the increasing duration of therapy. In common with others, in the early years we used streptomycin and PAS, in short, and often interrupted, courses, and even with the introduction of isoniazid the average course of chemotherapy was under six months. It is interesting to note that of 16 patients in our series who have shown relapse or failure of therapy, 14 occurred before 1955, and nearly all would now be considered as having had quite inadequate chemotherapy. Seven of these patients did, in fact, show satisfactory and apparently permanent healing on subsequent resumption and prolongation of therapy. Streptomycin (1 g. daily) was included as a routine in our earlier regime but, in view of its potential toxicity, its apparent tendency to heal by fibrosis, and the success of a combination of PAS and isoniazid, we now reserve streptomycin for operation cover, or for patients who do not appear to respond to PAS and isoniazid, or who, for some reason, cannot tolerate one or other of these drugs. Our routine treatment is therefore PAS, 10 to 15 g., with isoniazid, 200 to 300 mg. daily, and this is given during hospital residence, and for a long period thereafter. As with pulmonary lesions, the tendency has been towards longer duration of chemotherapy and it seems probable that most patients should take drug treatment for 1½ to 2 years to ensure effective healing and to prevent relapse. In hospital the PAS is given in a simple, fresh solution in water, and isoniazid in the usual 50-mg. tablets.

For outpatients and in the post-hospital period, we prescribe cachets containing both drugs to guard against the serious possibility of isoniazid being taken alone. With these drugs, as with streptomycin, difficulties often arise with toxicity or sensitivity reactions.

Sensitivity reactions to streptomycin and PAS are very common; those to isoniazid much less common. They may respond to the concomitant use of antihistamine products, and recently we have used cortisone with success. Desensitization by the administration of minute dosage—increased daily in the absence of further symptoms—is usually successful, and in difficult cases this desensitization can be carried out under cover of corticosteroids (Crofton, 1953; Sandler, 1955).

In recent months we have noted two cases in which recurring positive urine cultures have given rise to suspicion of failure of chemotherapy but bacteriological sensitivity tests have demonstrated bacillary resistance to isoniazid and in lesser degree to PAS. In one case the patient reported symptoms of gastric ulcer and admitted irregularity in the taking of PAS and isoniazid cachets. The other patient was given isoniazid alone by her chemist and presumably took that drug alone until her practitioner discovered the error.

These findings have raised in our minds the problem of bacillary resistance to the usual chemotherapeutic agents. Such resistance, of course, may arise from irregular or unsuitable therapy, but primary resistance has been experienced by many workers—due presumably to infection from a person who harbours resistant bacilli. That this is possible when the urogenital lesion develops seems entirely probable, and may well occur with slightly more frequency in future years. If sensitivity tests on cultures before chemotherapy is started, or later during treatment, show resistance to one of the three main drugs, the remaining two may of course be used, but resistance to two drugs will necessitate resort to one or more of the subsidiary drugs already used with some success in pulmonary lesions. Such drugs as pyrazinamide, viomycin, oxytetracycline, or cycloserine can usefully be employed, but require care in their administration, and are not very suitable for outpatient use.

Although we have reached the conclusion that prolonged therapy is essential, we are forced to recognize that cachets of PAS and isoniazid are often poorly tolerated, and that patients may fail to take these for the necessary lengthy period. By the routine use of a simple ferric chloride test for PAS in the urine, Simpson (1956) demonstrated that approximately 20 per cent. of patients attending the chest clinic failed to take the drugs prescribed. This is equally liable to occur in those who have suffered from urogenital lesions. Until a more acceptable and less toxic alternative to PAS is found, it would seem that the exact position should be discussed with all patients, and the importance of regular, full dosage, or a frank disclosure of failure to take cachets, be stressed. The results of the present regime which, particularly in genital lesions, have shown such a dramatic change over the years, and which we believe may reduce the necessity for surgical procedures even in moderate renal lesions, make it important to attempt to

obtain the fullest possible cooperation with general practitioners and their patients, and to attempt to ensure the best possible use of the available chemotherapeutic agents.

ANALYSIS OF CASES

Age and sex incidence.—In the present series the highest incidence of renal tuberculosis occurred in the 3rd, 4th and 5th decades in males, and in the 4th decade in females (table I). This is similar to the age distribution of pulmonary tuberculosis in the two sexes.

Decade	Males	Females	Total
10-20	6	6	12
20-30	22	10	32
30-40	21	17	38
40-50	30	6	36
50+	9	5	14
	88	44	132

TABLE I.—Age distribution of patients with genito-urinary tuberculosis.

The total period of *bed rest and of stay in hospital* is shown in fig. 1, and it will be seen that most patients were given complete bed rest for three to six months and remained in hospital for three to nine months. The transition from complete bed rest to more active participation in the social activities of the hospital is carefully graded.

The *operative interventions* undertaken in the tuberculosis hospital are shown in table II. These are complete except for one or two omissions where for one reason or another the operation had been done in the urological unit of the general hospital. In recent years the tendency has been to perform a total nephro-ureterectomy for widespread unilateral renal tuberculosis when the ureter is involved or stricture formation has occurred at its lower end. Ureterocolic anastomosis has been preferred to ileocystoplasty in persistent tuberculous ulceration of the bladder, when the remaining kidney has been threatened from backward pressure. In one patient with advanced hydronephrosis and hydroureter, ileal ureterostomy proved a satisfactory method of urinary diversion.

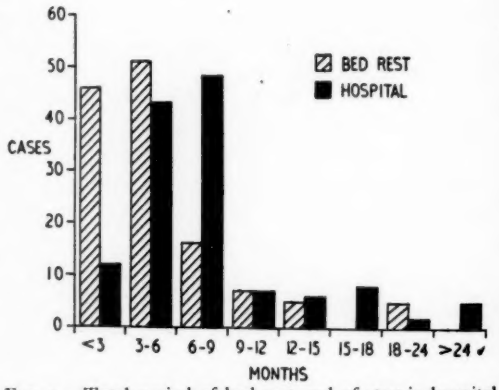

FIG. 1.—Total period of bed rest and of stay in hospital of patients with genito-urinary tuberculosis.

CLASSIFICATION

We have continued to use the following modification of the categories described by Jacobs and Borthwick (1950):—

(1) Tubercle bacilluria without pyelographic evidence of calyceal ulceration.
(2) Restricted unilateral renal tuberculosis.
(3) Widespread unilateral renal tuberculosis.
(4) Bilateral renal tuberculosis.
(5) Persistent or residual tuberculous cystitis.
(6) Genital tuberculosis.

DISTRIBUTION OF LESIONS

The distribution of the lesions is shown in table III. In the last three years we have noted that on the whole there would appear to be an increase in the number of admissions of patients with widespread unilateral disease of the kidney, whereas the proportion of patients with other types of genito-urinary lesions has remained relatively constant. This also applies to the association of renal with genital lesions in the male and the number of patients with renal lesions who had advanced tuberculous cystitis.

Nephrectomy	24	Epididymectomy	1
Nephro-ureterectomy	45	Cordotomy	1
Partial nephrectomy	1	Excision of hydrocele	1
Ureterocolic anastomosis	5	Cutaneous ureterostomy	1
Orchidectomy	3	Ileal ureterostomy	1

TABLE II.—Details of operative intervention in patients with genito-urinary tuberculosis.

Condition	Males	Females	Total
Bacilluria	14	8	22
Restricted unilateral	6	3	9
Widespread unilateral	42	25	67
Bilateral	9	5	14
Residual cystitis	5	2	7
Renal with associated genital lesions	50	—	50
Renal with associated cystitis			60

TABLE III.—Distribution of the lesions in patients with genito-urinary tuberculosis. Sixty patients with renal lesions had associated cystitis.

(1) *Bacilluria.*—We have considered that patients suffering from tubercle bacilluria should be given the benefit of adequate treatment by admission to hospital and by chemotherapy. The time for conversion of the urine to a negative culture was relatively short and most patients were able to return to work within a few months from discharge from hospital. The duration of chemotherapy has latterly been extended to a period of one year. The particulars relative to this group are given in table IV.

(2) *Restricted unilateral renal tuberculosis.*—This is a small but very interesting group of patients. Particulars relative to the group are given in table IV. Before the introduction of chemotherapy it was considered that even with minimal calyceal ulceration the lesions would continue to spread throughout the kidney, which would become caseo-cavernous and associated with a progressively severe ulcerative cystitis. The kidney, doomed to destruction, was removed at the earliest opportunity because of the toxic

manifestations associated with its presence and the need to protect the bladder. For a time following the introduction of chemotherapy partial nephrectomy under chemotherapeutic cover was the form of intervention practised by many surgeons with varying degrees of success (Semb, 1956). With growing confidence in conservative treatment in hospital with adequate and prolonged chemotherapy, it has been shown that the restricted unilateral renal lesion can heal spontaneously, and that partial nephrectomy has

	No. of cases	Frequency		Associated genital lesions	Associated cystitis
		On admission	On discharge		
Bacilluria	22	5	1	13	—
Restricted unilateral genito-urinary tuberculosis	9	4	1	3	3
Widespread unilateral genito-urinary tuberculosis	67	47	10	26	46
Bilateral genito-urinary tuberculosis	14	10	5	7	9
Residual cystitis in patients with genito-urinary tuberculosis	7	6	1	2	—

TABLE IV.—Analysis of cases of genito-urinary tuberculosis.

become an unnecessary operation in this type of lesion (Ljunggren, 1957). This is a revolutionary change in the management of early tuberculous disease of the kidney and very similar to the alteration in our management of pulmonary tuberculosis in which conservatism with chemotherapy has replaced the operative intervention.

Ljunggren, in 1957, described the operation of cavernotomy in which the excluded lesion of the kidney is evacuated by aspiration after which the outer shell is incised and the caseous material removed by means of a blunt curette or small swab. Streptomycin is applied locally to the cavity which is drained with a small polythene tube for subsequent daily instillations. This method of treatment of a localized tuberculous cavity has been described in greater detail by Tsuchiya *et al.* (1958) with most encouraging results.

Miss J.D., aged 19 years.—In August 1955 this patient had a tuberculous pleurisy and was treated in a sanatorium for a period of three months with chemotherapy. In April 1957, a restricted lesion of the middle calyceal system of the left kidney was recognized (fig. 2) and she was subsequently treated in a tuberculosis hospital by bed rest and with streptomycin, PAS and isoniazid. Within three months the restricted lesion in the left kidney completely resolved (fig. 3). Some months later, she reported well with no frequency, and had married.

(3) *Widespread unilateral renal tuberculosis.*—This group of 67 patients was the largest in the series. Not infrequently patients are found to have widespread renal disease before symptoms appear or before they seek admission to hospital. The particulars relative to the series are given in table IV. The operation of choice was nephro-ureterectomy with two incisions: the first a sub-umbilical midline approach to mobilize the lower third of the ureter extraperitoneally and to divide it just above the bladder;

thereafter the patient was turned on his side and the kidney and ureter were removed through a lumbar approach; the last rib was usually excised. Because of the frequency of associated genital lesions or cystitis, chemotherapy has been prolonged in this group for about two years.

(4) *Bilateral renal tuberculosis.*—This is a small series but unfortunately the lesions occurred in a young age-group, the majority males. In these young men associated genital lesions were common, and accompanied by

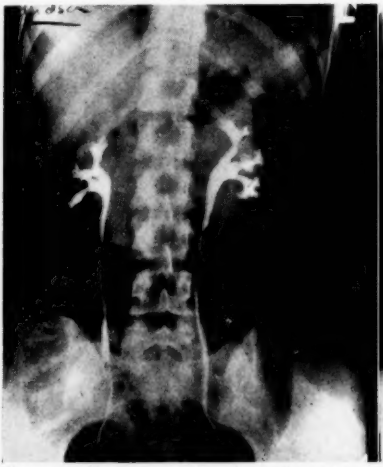

FIG. 2.—Pyelogram showing ulcerative calyceal lesion of middle major calyx system of left kidney.

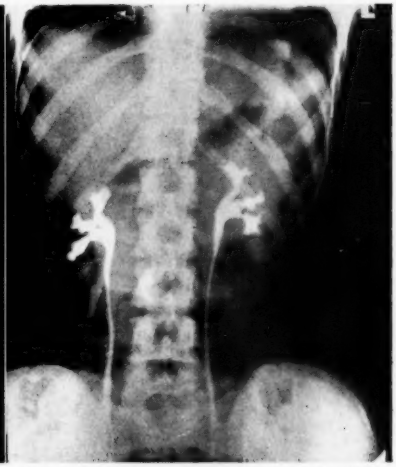

FIG. 3.—Same patient three months later, after hospital treatment and chemotherapy. The middle calyceal lesion of the left kidney has healed.

cystitis in nearly every case. All achieved conversion of the urine in six months and over half the patients were able to return to some form of employment. In all, chemotherapy was continued for at least two years. In the operative treatment of these patients, the more seriously diseased kidney was removed in seven cases. The relative particulars concerning this group are shown in table IV.

(5) *Residual cystitis.*—These were patients who were readmitted on account of reversion of the urine and recurrent tuberculous ulceration of the bladder. It was considered that in all patients in this group inadequate chemotherapy had been given at an earlier stage in their treatment. Five of the patients had been treated elsewhere. Because of backward pressure in the remaining kidney, ureterocolic anastomosis was carried out in five, and ileal ureterostomy in one. The majority of the patients achieved conversion of the urine and a negative culture for tubercle bacilli and about half of them were able to return to a modified form of employment within a year after discharge from hospital. The relative particulars are shown in table IV.

(6) *Genital tuberculosis in the male.*—There were 62 cases of genital

tuberculosis, and the distribution of the lesions is shown in table V. We have always taken the opportunity of carrying out a bimanual examination when the patient was cystoscoped under thiopentone anæsthesia. The value of the information obtained from the rectal examination with the patient fully relaxed is shown from the number of occasions on which it was possible

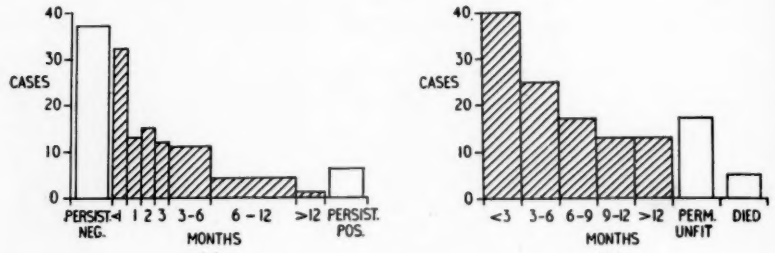

FIG. 4.—Conversion period for all cases of genito-urinary tuberculosis (a), with period of delay before return to work after discharge (b).

to recognize lesions in the seminal vesicle or the prostate. Sinus formation in the scrotum occurred in 19. We would stress the fact that out of 62 cases of genital tuberculosis in the male, orchidectomy was considered necessary in only three, and epididymectomy in only one patient (see table

	Cases	Percentage
Epididymis	43 (12)	70 (20)
Seminal vesicle	37 (3)	60 (5)
Prostate	40 (9)	64 (15)
Combined genital lesions	38	61

TABLE V.—Genital tuberculosis in the male: distribution of lesions in 62 cases.
(Figures in brackets indicate sole lesion)

II). There can be no doubt that the scrotal lesion with sinus formation will heal under conservative measures alone. The response to chemotherapy, bed rest with a scrotal support, and aspiration when necessary, is quite dramatic. In the majority of the patients there was conversion of the urine, or of the discharge from the scrotal sinus in one month. Chemotherapy was continued until the epididymis had shrivelled to a fibrous strand and pelvic lesions could no longer be detected on rectal examination. In our experience, patients with genital lesions require the same hospital management and prolonged chemotherapy as those with pulmonary or restricted renal lesions. We have been most impressed with the response of these lesions to conservative measures without resort to surgery.

EFFECT OF TREATMENT

With the general scheme of treatment described—with admission to hospital, bed rest, chemotherapy, and operative intervention when necessary

—it has been found that the conversion period for the majority of patients when the culture for tubercle bacilli became negative, was within three months of admission to hospital (fig. 4a). Most patients were in hospital for eleven weeks before operation and subsequently for about twenty weeks.

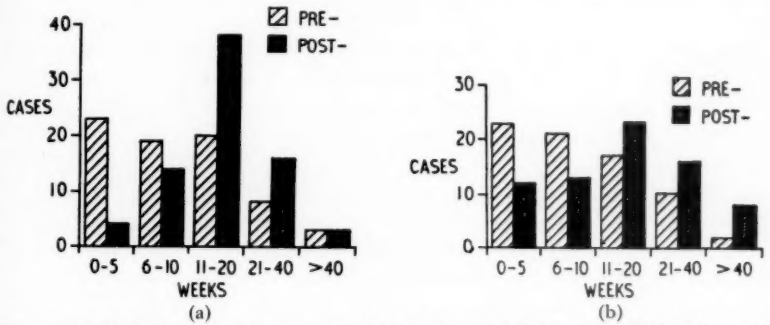

FIG. 5.—Period of pre- and post-operative stay in hospital (a), and period of pre- and post-operative chemotherapy (b), for patients with genito-urinary tuberculosis.

Figure 5 shows the complete period of stay in hospital, but as regards the average period of pre- and post-operative chemotherapy we have found in the light of our experience during the last five years that the majority of patients are subjected to chemotherapy for a period of one to two years. The majority of the patients have returned to work within three months of discharge from hospital: the proportion of those permanently unfit for resumption of work has been small (fig. 4b).

In this series of 132 patients suffering from urogenital tuberculosis the over-all mortality in a five-year follow-up has been 3.8 per cent. The proportion unfit to return to work has been 13.6 per cent., and we have been gratified to find that 82.6 per cent. of our patients have been able to return to employment within a reasonable interval after their discharge from hospital. In a small series of 41 cases which we personally followed up between 1935 and 1940, the late mortality rate was 24.5 per cent., and 39 per cent. remained permanently unfit. This contrast is quite remarkable and a tribute to the efficacy of chemotherapy in tuberculosis.

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DRUG-INDUCED RENAL DISEASE

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Iatrogenic disease (*Iatros* = the physician) is a new name for an old idea. Throughout the history of medicine there have been many examples of induced disease or of death consequent upon therapeutic endeavour. Attempts to influence favourably the natural history of illness are sometimes attended by the emergence of features which would not otherwise have arisen, and this is becoming increasingly true as therapy becomes both more effective and more complex.

CLASSIFICATION

These diseases may affect almost every system in the body and may result either from the administration of drugs or from the application of surgical measures, simple or complex. On *a priori* grounds it might be supposed that the kidneys would be particularly exposed to the unwelcome actions of drugs. Approximately one-fifth of the total cardiac output flows through these organs, which themselves represent only about one two-hundredth of the body weight. They might thus be presented with an amount of drug far in excess of that delivered to the brain, heart or liver. Furthermore, they represent the channel of excretion of the majority of drugs used in clinical practice, and by the process of selective reabsorption of water the renal tubules are exposed to a concentration which may be many times that present in the systemic blood. In spite of these facts, however, drug-induced renal diseases are relatively uncommon and the kidneys take third place to the bone marrow and the liver in their susceptibility to undesirable pharmacological effects.

The mechanisms by which abnormalities in renal structure or function are produced by pharmacological agents are complex and poorly understood. Systematization of the toxic actions of drugs has barely begun and rational toxicology is not yet an organized division of pharmacology. Although attempts are being made to discover the precise mode of action of drugs in this respect (Barnes, 1957), they are not sufficiently advanced to permit a classification or analysis of drug-induced renal disease other than in the most general biological terms.

It is the purpose of this article to consider only those disorders which may arise in the course of drug therapy, omitting reference to renal damage from poisoning with large amounts of drugs taken with suicidal intent or by accident. These diseases may be considered to fall into four groups:—

(1) Diseases arising from the administration of drugs in doses in excess of therapeutic requirements.

(2) Diseases produced by drugs whose therapeutic dose closely approaches, or is similar to, the toxic dose.
(3) Diseases arising from abnormal reactions to therapeutic doses of drugs; i.e. idiosyncrasy and hypersensitivity.
(4) Diseases produced by drugs which lead to renal lesions by indirect means.

DISEASES ARISING FROM THE ADMINISTRATION OF DRUGS IN EXCESS OF THERAPEUTIC REQUIREMENTS

The milk-alkali syndrome.—This syndrome is a disorder in renal function which arises in the course of prolonged treatment with absorbable alkalis and milk in patients suffering from dyspepsia and peptic ulceration. The condition was first recognized by Hardt and Rivers in the United States in 1923, and similar patients were soon described in this country. The classical picture is one in which malaise, personality change and mental confusion are associated with features of renal failure. These include polyuria, thirst, anæmia, proteinuria, elevation of blood urea, impairment of concentrating and diluting power, and, in severe cases, hypertension. The majority of patients give a history of drinking one pint (570 ml.) to two quarts (2,280 ml.) of milk per day, and all patients admit to taking moderate or large amounts of absorbable antacids. The most important of these is sodium bicarbonate—often taken in the form of Sippy powders. Serum calcium concentration is usually increased and this appears to be related to the high calcium intake from both milk and antacids such as calcium carbonate.

It is difficult to be certain of the precise mechanism of the renal failure in the milk-alkali syndrome. Originally, alkalosis itself was considered to be resonsible for the depression of renal function leading to uræmia.

This view was supported by observations such as those reported by McCance (1937), in which severe uræmia occurred consequent upon the alkalosis of prolonged vomiting. Sanderson (1954), however, has recently challenged this concept; he failed to induce renal damage by the production of acute alkalosis in patients given very large amounts of sodium bicarbonate over periods of some weeks. Indeed, in his subjects the urea clearance increased and the blood urea concentration fell during the development of alkalosis in which the blood bicarbonate content increased by 7 mEq/l. On the basis of these observations Sanderson suggested that the nephropathy seen in clinical alkalosis is not due to the disturbance in acid-base balance itself, but is the consequence of diminished renal blood flow due to water and salt depletion with the development of tubular necrosis from renal ischæmia.

Although these hæmodynamic factors are undoubtedly important in patients in whom vomiting is severe, it is difficult to believe that they are operative in the majority of patients suffering from the milk-alkali syndrome. Most of the cases reported in the literature do not appear to have been significantly depleted of water and salt, and vomiting was minimal, at least in the initial stages.

Cope (1936) was among the first to describe the elevation in the concentration of blood calcium in this syndrome, and the known deleterious effect of hypercalcæmia and hypercalcuria on renal function suggests that

this might be an important factor in the depression of renal function. Certainly nephrocalcinosis has been described in some patients with this disorder (Cooke, 1932). In view of the known limitation of intestinal calcium absorption it seems unlikely that excessive calcium intake is the sole cause of the calcium deposition, but a combination of hypercalcuria and alkalosis might well be responsible. Mulligan (1946, 1947) has pointed out that calcium precipitation is favoured in tissues where acids are formed under normal circumstances, and which are themselves presumably rendered alkaline (e.g. the gastric mucosa and the renal tubules). Calcium precipitation in the kidneys might thus be encouraged by the formation of an alkaline urine over long periods of time.

Although the diagnosis of the milk-alkali syndrome is not usually difficult, the condition has been confused with chronic nephritis, hyperparathyroidism and pyloric obstruction. The finding of an elevated serum bicarbonate concentration is of great value in the diagnosis, as this blood constituent is either normal or reduced in hyperparathyroidism and chronic nephritis. A diet low in calcium and the withholding of alkali therapy result in rapid improvement. Renal function returns to normal in all but a few, who progress to irreversible renal failure (Burnett *et al.*, 1949; Kyle, 1954).

Vitamin intoxication.—The daily requirements of vitamin D are now assessed as being about 400 i.u. Over-prescribing or self-medication with potent preparations of vitamin D may result in the consumption of several hundred thousand units a day and the development of signs of intoxication. Probably for the reasons already given, the kidneys are especially vulnerable to vitamin D intoxication, and parenchymal calcification is common in these organs. The calcium appears to be deposited first in the cells of the convoluted tubules but is later found in the glomeruli and the walls of the arcuate, subarcuate and interlobular arteries in severe cases. Radiological demonstration of nephrocalcinosis is sometimes possible and its presence can be demonstrated in renal biopsy specimens (Brun *et al.*, 1953).

Symptoms of vitamin D intoxication include such features as headache, vomiting, abdominal pain and diarrhœa. Renal manifestations are often early and consist of polyuria, nocturia and thirst. Impairment in renal function may be progressive and uræmia develops. Proteinuria is invariably present, but rarely marked. In severe cases hypertension develops. Intoxication with vitamin D may occur in patients suffering from osteomalacia arising in a variety of diseases, where its administration has been excessive. Such intoxication is particularly liable to develop in patients with renal osteodystrophy in whom there is a significant degree of hyperparathyroidism in addition to osteomalacia. The vitamin may rapidly reduce bone pain in these circumstances, and its use should be controlled carefully by repeated determinations of serum calcium (Stanbury, 1957). The majority of patients suffering from hypervitaminosis D, however, have received large doses of the vitamin for the treatment of conditions not due to vitamin D deficiency.

These include rheumatoid arthritis, tuberculosis and asthma. There is now little justification for the continued use of vitamin D in these conditions.

Of considerable national importance is the relationship of *idiopathic hypercalcæmia of infancy* to vitamin D intoxication. The clinical, chemical and pathological findings in this uncommon syndrome closely resemble those found in unequivocal vitamin D intoxication. All infants reported as suffering from the syndrome have been artificially fed with fortified infant food with or without vitamin D supplement. A few months after birth such children develop anorexia and vomiting, with thirst and polyuria, and fail to gain weight. Elevation of blood urea and serum calcium concentration occur, and there is depression of the glomerular filtration rate and the urea clearance (Stapleton, MacDonald and Lightwood, 1957). At the present time, with conscientious use of the welfare foods, including cod-liver oil, and of vitamin D reinforced cereals, it is possible for a mother to give her child up to 4000 i.u. a day. It therefore appears possible that this disease of infancy may be a simple intoxication which manifests itself in only a very small number of children; those affected may lie on the extreme fringe of the normal distribution curve for the population in regard to their responsiveness to vitamin D and hypercalcæmia.

Mercurial and other heavy metal poisoning.—Mercury, gold, arsenic, bismuth and thallium are metals which in one form or another are of some value in therapeutics and which are capable of producing severe renal disease when given in excess. The renal lesion consists of tubular cell necrosis and has been most adequately studied in the case of mercury intoxication. Microdissection of individual nephrons shows that the necrosis occurs mainly in the proximal tubules (Oliver, MacDowell and Tracy, 1951) and may be due to the reabsorption of water locally raising the concentration of mercury. The glomeruli appear normal. Characteristically, proteinuria is the first manifestation of renal damage and may be so severe that the nephrotic syndrome develops (Burston, Darmady and Stanack, 1958). It is uncertain whether the proteinuria is the result of increased filtration of protein by the glomerulus or of diminution in tubular reabsorption.

Mercury poisoning with renal failure has been described in numerous patients following the use of organic mercurial compounds (Munck and Nissen, 1956; Riddle *et al.*, 1958), although its incidence is extremely low. In the majority of these cases large doses of organic mercurials have been given over prolonged periods of time and in some of the patients the administration has been continued in spite of the development of resistance to the drug. Persistent administration of mercury in the absence of diuretic response is dangerous but serious consequences may be avoided either by taking steps to re-establish sensitivity to the drug by the administration of ammonium chloride, potassium, or aminophylline, or by the use of an alternative diuretic.

Despite the fact that there is no clear evidence of the therapeutic value of gold, it continues to be widely used, and as many as 50 per cent. of patients receiving gold are alleged to show at least a trace of protein in the urine at some time during therapy (Goodman and Gilman, 1955). As with mercury, gold nephrosis occurs usually after prolonged therapy, and is rare (Kuipers, 1953).

Pain-controlling drugs.—Apart from frank poisoning from accidental or intended ingestion of large amounts of drugs, renal effects of intoxication with analgesic and antipyretic drugs are uncommon. Phenylbutazone is well known to produce water and salt retention and œdema in therapeutic doses, but severe renal failure probably occurs only when the drug is given in excess or over long periods of time. In these circumstances tubular necrosis develops and anuria and death may occur (Lipsett and Goldman, 1954; Scheitilin and Jeanneret, 1957). It seems reasonably certain also that recently reported fatalities with renal involvement due to phenacetin (Zollinger, 1955) were the result of excessive dosage. Tubular necrosis with anuria may result also from gross overdosage with salicylates (Campbell and MacLaurin, 1958). When given in therapeutic doses, especially to infants, however, complex acid-base disorders due to a combination of respiratory alkalosis consequent upon stimulation of the respiratory centre, and a metabolic acidosis due to the renal excretion of bicarbonate, may develop (Singer, 1954; Heymann *et al.*, 1954).

DISEASES PRODUCED BY DRUGS WHOSE THERAPEUTIC DOSE CLOSELY APPROACHES THE TOXIC DOSE

The distinction between the drugs in this category and those already discussed is simply one of degree. For the most part the drugs involved are antibacterial substances.

The sulphonamides.—The sulphonamide group of drugs may be responsible for renal disease in a variety of ways. Most commonly there is no question of hypersensitivity: renal damage with oliguria or failure occurs simply as a result of deposition of crystals of the acetylated derivatives in the renal tubules, ureters or even in the urethra (Prein, 1945; Miller and Mitchell, 1952). Although such complications were common with sulphapyridine and sulphathiazole, they have become extremely rare in clinical practice and are almost unknown when sulphadimidine is used. Recently, this complication of sulphonamide therapy has again gained prominence by reports of hæmaturia, oliguria and anuria occurring as a result of treatment with sulphamerazine, either by itself (Arneil, 1958) or in combination with other sulphonamide compounds (Arneil, 1958; Aitkinson, 1957; Browne, 1957). It is significant that the solubility of both sulphamerazine and acetyl-sulphamerazine is about half that of sulphadimidine in the acid range of urine pH. Deposition of crystals does not appear by itself to produce any lesion in the kidney other than obstruction to urine flow. Even with sul-

phadimidine a reasonable flow of urine should be maintained during therapy, and the development of renal colic or the finding of red blood cells in the urine is sufficient reason for reducing or stopping treatment and alkalinizing the urine. Sulphonamide crystals found in the cooled urine of patients under treatment are by themselves of no significance.

Neomycin, bacitracin, polymyxin B and streptomycin.—Neomycin, bacitracin and polymyxin are nephrotoxic and this danger is so great in the case of neomycin as to preclude its parenteral use. Already some fifteen necropsy reports have appeared in the literature of patients who have died following neomycin therapy and in whom this drug has contributed to death from renal failure (Powell and Hooker, 1956). Severe tubular damage with necrosis is common, and casts form in the tubular lumina. Renal damage is indicated during life by the appearance of proteinuria and granular casts in the urine, and uræmia develops in some patients. The damage may be severe enough to result in anuria. Although these abnormalities usually subside rapidly on cessation of therapy, they occur so often that the use of neomycin should be confined to topical application, or oral administration for purposes of intestinal antisepsis.

Bacitracin and polymyxin are both polypeptides capable of reducing renal function and producing organic renal changes. Both drugs probably owe their toxicity to their amino-acid content, and similar lesions may be produced experimentally by compounds such as *d,l*-serine (Wachstein and Meisel, 1954).

In a series of twelve normal male subjects, parenteral administration of bacitracin uniformly resulted in proteinuria and the appearance of casts in the urine and often in glycosuria (Miller and MacDonald, 1950). An acute depression in the rate of glomerular filtration, renal blood flow, and the capacity for maximal tubular reabsorption of glucose was observed following parenteral administration of bacitracin in therapeutic doses.

Necropsy examination reveals tubular degeneration and necrosis, with swelling of proximal tubular cells, the glomeruli being unaffected (Jenkins, Uhr and Bryer, 1954). Similar abnormalities have been shown to occur with polymyxin B (Moyer *et al.*, 1953). It seems clear from these observations that bacitracin and polymyxin B should be used systemically only in the treatment of serious disease not amenable to other remedies.

In the early days of streptomycin therapy proteinuria with the appearance of casts in the urine was common. Occasionally it was severe enough to necessitate the cessation of therapy. With the purer preparations now in use this complication appears to be practically unknown.

DISEASES ARISING FROM ABNORMAL REACTIONS TO THERAPEUTIC DOSES OF DRUGS

Although idiosyncrasy and hypersensitivity are not identical states, it is convenient to group together those renal disorders which arise in a small group of the population as the result of an abnormal reaction to a drug,

irrespective of whether this is due to hypersensitivity. With the establishment of the fact that relatively simple chemical compounds may act as specific antigens, it has now become apparent that certain chemical configurations possess higher degrees of antigenicity than others. Those compounds in which a benzene ring serves as a nucleus to which an amino-group is attached (sulphanilamide, procaine, para-aminosalicylic acid), or substances in which the pyrimidine nucleus is present (thiouracil, mesantoin, sulphadiazine), are particularly liable to produce serious hypersensitivity reactions. Characteristically, sensitivity reactions to drugs follow certain common patterns and in so far as they involve the kidney they take two forms: polyarteritis nodosa and nephrosis (Alexander, 1955).

Polyarteritis nodosa.—Polyarteritis nodosa was first described in 1866 and up to 1931 there were only about 200 proved cases in the world literature. Since then many thousands of patients have been treated for this condition. Although this increased frequency is undoubtedly due partly to a higher threshold of suspicion and to the development of improved diagnostic techniques such as muscle, skin and renal biopsy, it has been used as evidence to support the view that in some patients the condition is due to a hypersensitivity reaction to drugs formerly unavailable.

During the course of the illness characteristic necrotizing lesions involving arteries and arterioles may develop in almost any organ in the body and the kidneys are involved in a high percentage of cases. The extent of the renal involvement largely determines the outlook in individual cases as renal failure and hypertension are the most common causes of death (Lovell and Rose, 1955). Histologically, the renal lesions take the form of either polyarteritis of the renal vessels or glomerulitis, described first by Davson, Ball and Platt (1948). Protein, red blood cells, and granular, hyaline or cellular casts may appear in the urine intermittently. Diagnosis during life is made in about 50 per cent. of cases and should be suspected by the diffuseness of organ involvement, the elevated erythrocyte sedimentation rate, hypertension, fever, respiratory symptoms, joint features and urinary abnormalities. In a few instances the illness can begin like acute glomerulonephritis, with hæmaturia and œdema. Hypertension is absent at this early stage and this feature may suggest the true diagnosis.

The idea that in man polyarteritis may be due to drug hypersensitivity is widely accepted.

The view springs mainly from the demonstration of arteriolar lesions in experimental animals sensitized to various proteins and horse serum (Rich and Gregory, 1943) and from the presence of similar lesions in human patients who are alleged to have developed the disease as a result of the administration of sulphonamides (Rich, 1942), iodine (Rich, 1945), thiouracil (Dalgleish, 1952), neoarsphenamine (Miller and Daley, 1946), DDT (Hill and Damiani, 1946), sodium dilantin (Van Wyke and Hoffman, 1948), and penicillin (Waugh, 1952).

Rose and Spencer (1957) have recently discussed critically the evidence in favour of the view that in some patients this disease is drug induced.

Although a history of taking sulphonamides is common in such patients, this is by no means invariable and the subsequent development of polyarteritis might well be related to the preceding infection, usually a respiratory one, for which the sulphonamide was given. The evidence implicating thiouracil as a cause of polyarteritis is stronger than that for sulphonamide as there is little evidence to suggest that thyrotoxicosis is in any way related to this disease. The question as to whether polyarteritis nodosa is a iatrogenic disease is thus still *sub judice*. Although accepted as such by the majority of clinical workers, a final decision, as pointed out by Rose and Spencer, will be obtained only by clinical investigation planned in advance. Retrospective studies and individual case reports have served their function by raising questions but will not themselves provide solutions.

Nephrosis with heavy proteinuria has been described on numerous occasions following treatment with trimethadione (White, 1949) and paramethadione (Wren and Nutt, 1953). Lesser degrees of renal injury with proteinuria also commonly follow treatment with aloxidone, which chemically closely resembles trimethadione (Millichap and Kirman, 1953). The rarity of these reactions among the many thousands of patients treated for years with these drugs suggests that the response is due to either allergy or idiosyncrasy. Histologically, necrosis of the renal tubules is found. Similar consequences may follow from the administration of sulphonamides, when the renal lesions do not appear to be related to crystal deposition and are distinct from those of polyarteritis nodosa (Allen, 1951). Similar reactions have been described also with the sulphonamide derivative, acetazolamide (Glushein and Fisher, 1956).

DISEASES PRODUCED BY DRUGS WHICH LEAD TO RENAL LESIONS BY INDIRECT MEANS

In all of these conditions the mechanism involves a drug-induced abnormality which in its turn and of its own accord disturbs renal function.

The nephropathy of potassium depletion has been recognized only recently as a distinct clinical entity. Experimental potassium depletion has been known for many years to result in renal tubular lesions (Schrader *et al.*, 1937). Although the syndrome may arise from any condition resulting in excessive loss of potassium it is most commonly drug-induced by chronic over-indulgence in, or over-prescription of, cathartics of the more vigorous type such as cascara sagrada, aloin and phenolphthalein. The chronic diarrhœa thus induced, even if punctuated by periods of constipation, is sufficient over the years to deplete the body of approximately one-quarter or more of its potassium content. The prolonged use of cortisone without potassium supplement has also been known to result in the syndrome. Relman and Schwartz (1955) were among the first to draw attention to the clinical manifestations and to the renal lesion. The clinical features of potassium depletion are often overshadowed by the primary disease but in

so far as they involve renal function they consist of thirst, polyuria and hyposthenuria. Small amounts of protein and granular casts are found in the urine. There is a decrease in glomerular filtration rate, but elevation of blood urea nitrogen is minimal. The thirst and polyuria may be so severe as to raise the possibility of diabetes insipidus in the differential diagnosis. Renal biopsy studies reveal vacuolization in the renal tubules which subsides when the potassium depletion is corrected.

Renal calculi.—Renal complications of malignant disease of the blood cells and reticuloendothelial system are rare (Merrill and Jackson, 1943). In some cases, however, such complications occur as a result of treatment with cytotoxic drugs such as nitrogen mustard. The destruction of malignant cells necessarily results in the breakdown of nucleoproteins with the ultimate formation of purines which are oxidized to uric acid. If this is excessive, and especially if the urine is acid, crystallization and renal stone formation with urinary obstruction may develop (Richmond and Beardsley, 1953). A similar complication following radiotherapy has been recognized for many years (Lear and Oppenheimer, 1950). Although elevation of the uric acid concentration in the blood is commonly seen with both forms of therapy, the development of renal calculi occurs in only a very small percentage of cases.

Hypotensive drugs.—The susceptibility of the kidneys to damage from hypotension and circulatory failure is well documented experimentally and clinically, and is separately discussed in this symposium by Professor Bull (1958). Fortunately, development of acute tubular necrosis is seen only very infrequently during the course of treatment with hypotensive drugs. Two such cases have been reported recently with pentolinium tartrate (Carter and Payne, 1956).

> In one case the drug was used satisfactorily for fifteen months in an elderly patient and the usual signs of overdosage, i.e. postural vertigo, constipation and dryness of the mouth, were absent when oliguria with hypotension developed. In the other, a relatively large initial dose of pentolinium was given to a patient of unknown sensitivity.

Similar episodes have been described with 'controlled' hypotension in surgery (Hampton and Little, 1953). A recurrence of such accidents would seem to be avoidable if oliguria is recognized as a sign of possible overdosage with hypotensive drugs in elderly patients, if the sensitivity of the individual to the drugs is established initially, and if renal function is measured at intervals during therapy, especially among those who already suffer from some degree of renal impairment.

Osmotic nephrosis.—The occurrence of osmotic nephrosis was first noted around 1940 when the intravenous injection of hypertonic sucrose was widely used to reduce cerebral or generalized œdema. Swelling and vacuolization of the cells of the proximal tubules are prominent histological features. Similar changes have been found following the administration of hypertonic solutions of other substances such as xylose, insulin, acacia, creatinine and

glucose. These renal lesions have not, for the most part, been accepted as producing clinically detectable abnormalities in renal function and have been attributed by Allen (1951) to imbibition of fluid by the epithelial cells, consequent upon the increased osmotic concentration within the proximal tubular lumen. In 1953, however, Golden and Prior reported the death from uræmia of a patient with Laennec's cirrhosis who had been given hypertonic glucose for ten days and in whom similar histological changes in the kidneys were found at necropsy. The relationship of the administration of hypertonic glucose to the renal histological changes and to the clinical picture found in patients who have died in hepatic coma clearly requires further investigation.

CONCLUSION

Sufficient has been said to indicate the complexity of the mechanisms of drug-induced renal disease. Fortunately these disorders are uncommon and the remarkable physiological ingenuity of the kidney would seem to be matched by its relative pharmacological insusceptibility to toxic damage.

Nevertheless, iatrogenic renal disease occurs sufficiently often to present a challenge both to the physician and to the pharmaceutical industry. The doctor must avoid the error of interpreting drug-induced clinical abnormalities as part of the natural history of the underlying disease. The pharmaceutical industry, on the other hand, bears the burden of the need to test new drugs for both acute and chronic toxicity. Public safety in this regard is not protected by enforced registration of such toxicity tests. This imposes upon the industry a need for a sense of responsibility and integrity which could probably not be attained by legislation in any case. Apart altogether from the necessity to develop ever less toxic therapeutic agents, close cooperation between the drug industry and the clinician in the use of properly constituted clinical trials should do much to reduce the incidence of iatrogenic disease in the future.

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THE PRESENT STATUS OF RENAL RADIOLOGY

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It is now more than sixty years since the discovery of x-rays. At first only the thinnest parts of the body could be examined, but by the beginning of the century radiography of the abdomen had become an established procedure in the hands of those few pioneers who had the vision to perceive the possibilities of this new method of examination. The demonstration of calcified opacities in the renal areas thus became possible, and experience rendered the differential diagnosis of calculi from other shadows more and more accurate.

DEVELOPMENT OF UROGRAPHY

In 1906, thanks to the recent introduction of the first practical cystoscope, Voelcker and von Lichtenberg were able to demonstrate the outlines of the renal pelvis and calyces by the injection of a contrast medium up the ureter. Although this was but a logical step following the use of bismuth in the examination of the gastro-intestinal tract, it was to be the last major advance in radiography of the kidneys for more than a quarter of a century. It was responsible, however, for the basis of much of our present knowledge of radiology of the urinary tract, and during this period enormous strides were made in the surgery of this region.

Nevertheless, the need for some simpler method became increasingly apparent. Many surgeons did not possess the necessary equipment or skill to embark upon this form of examination and indeed many pathological conditions in the bladder and ureters rendered it difficult or impossible. The physicians, likewise, demanded some simple procedure as an aid to their diagnosis of abdominal and systemic disorders. They were encouraged in those hopes by the introduction of tetraiodophenolphthalein by Graham and Cole, in 1924, as a medium for cholecystography.

It was found that iodine compounds were excreted fairly readily by the kidneys and the high atomic number of the element rendered it opaque to x-rays. Several intravenous compounds were tried in the years 1926-29, and it was found that, whilst some of these gave adequate detail in the kidneys, their relatively high toxicity rendered them unsuitable for general use. In 1929, Binz and Raeth, after trying many substances, introduced 'uroselectan', which was shortly superseded by 'uroselectan B'. This was injected intravenously and details of excretion became visible within five minutes, reaching their maximum in the kidneys after about half-an-hour. Side-effects from the use of this drug were uncommon except that it caused intense pain and sloughing when accidentally injected into the soft tissues,

whilst its occasional introduction into an artery or nerve resulted in the loss or paralysis of the distal portion of the limb. Its use constituted a new era in diagnosis. A later development in contrast media was diodone, which was non-irritant and could even be injected subcutaneously. This became the drug most commonly used for some fifteen years. X-ray detail was similar to that with 'uroselectan B', and the only disadvantage was occasional nausea and vomiting with more severe reactions in allergic individuals. Newer preparations have a higher number of iodine atoms in the molecule and improve the radiographic detail considerably, at the same time reducing substantially the number and severity of the side-effects.

So far there is no satisfactory oral contrast medium for urography and, on account of the slow absorption from the gut and the rapid excretion once it has reached the tubules of the kidney, it seems unlikely that one will be developed for general use.

This, in brief, is the history of the development of urography which remains the most important single examination in the study of renal disease. With a properly prepared and dehydrated patient modern intravenous compounds generally give excellent detail in the kidneys. This can be enhanced considerably by the use of ureteric compression by means of a bag or balloon tightly strapped across the lower abdomen. If the compression band is attached to a plastic plate below the patient oblique views may be taken. By using this technique a retrograde examination will seldom be required, thus lessening the risk of dissemination of the disease when it is of tuberculous origin.

AORTOGRAPHY

Aortography is a spectacular and important method of investigation and is being increasingly used throughout the country.

In its original form it is best carried out with the patient under a general anæsthetic. He is placed on the x-ray couch in the prone position, and the needle is inserted about 8 cm. to the left of the midline, just below the 12th rib. It is directed cranially and medially until it impinges on the vertebral body. It is then withdrawn a little and adjusted so that it passes as close as possible to the body of the vertebra as it is advanced into the aorta which lies in front. About 30 ml. of a highly concentrated contrast medium are then injected very rapidly, preferably with a special apparatus. By means of a serial changer several radiographs are then taken in quick succession. This device may be quite simple or very elaborate indeed, but should permit of four or five films being exposed in the same number of seconds.

More recently another method of aortography has been described by Seldinger (1953), whereby a catheter is introduced into the femoral artery under local anæsthesia and is passed up until the tip lies above the origin of the renal arteries. The contrast medium is then injected rapidly and the serial radiographs taken.

When properly performed either technique gives a clear picture of the renal arteries and their branches. Their size, course and distribution are shown in the early serial films, whilst the later filling of the capillaries and veins demonstrates vividly the outline of the whole kidney parenchyma.

It is in the differential diagnosis of renal neoplasms and cysts that aortography is particularly useful. In the case of a cyst the renal arteries are displaced and stretched over it whilst the mass itself is avascular. In the case

of a hypernephroma, however, whilst there may be some displacement a rich network of vessels is demonstrated and the later films show 'pooling' of the contrast medium within the growth itself. Until recently a normal urogram was thought to free the kidneys from any suspicion of neoplastic involvement. Lofgren (1954) and Olhagen (1954), however, report instances in which the urographic appearances were entirely normal but the clinical evidence pointed otherwise. In two cases aortography revealed the presence of a hypernephroma. In Olhagen's case no less than six urographic examinations were reported negative. This of course does not suggest that urography should be replaced, but urologists may in future request aortography more often in cases in which there is no obvious cause for renal hæmorrhage.

In cases of hydronephrosis, aortography is of value in determining whether there is sufficient renal parenchyma present to justify preserving the kidney or whether nephrectomy is indicated. In renal tuberculosis the defective blood supply to the involved area is clearly demonstrated by aortography. When a partial nephrectomy is contemplated the demonstration of the arterial tree can prove of value to the surgeon when planning the operation. When hypertension is present aortography is useful in assessing the size of the renal arteries, and the lack of homogeneity, or spotted appearance, in the nephrogram is an indication of the degree of damage to the renal parenchyma. When the changes are unilateral, nephrectomy sometimes results in considerable improvement of the hypertension. In cases of agenesis and renal ectopia, in which the pyelogram fails to show the presence or position of the kidney, an aortogram may relieve the patient of the necessity for an operation. When hydronephrosis is believed to be due to an aberrant vessel the combination of an aortogram with excretion urography is of assistance in demonstrating the artery concerned, thus making a positive preoperative diagnosis and facilitating the operation itself. In polycystic disease of the kidneys, excretion urography or, when the contrast is very poor, retrograde pyelography is usually sufficient to make the diagnosis but, when the cysts are not large, aortography is of help in showing the renal outlines and the small and widely separated terminal branches of the renal artery which sometimes curve round the walls of the larger cysts. The nephrogram demonstrates the degree of destruction in the substance of the kidney.

A further refinement of aortography by the catheter method has been the introduction, by Odman (1956), of selective catheterization of the renal artery. For this purpose a specially shaped opaque catheter is used and can be manipulated into the renal artery under fluoroscopic control. For this purpose the image intensifier is invaluable as it allows the work to be carried out with a certain amount of room lighting and with much greater image clarity than would otherwise be possible. The reduction in the amount of x-rays received by the patient and operator is also an important factor. Greig, Allcock and Berridge (1957), in England, and Frimann-Dahl (1958), in Norway, have obtained good results by this method and have been able to use small amounts of a lower concentration of contrast medium.

DANGERS OF AORTOGRAPHY

Despite the undoubted importance of aortography in the radiological diagnosis of renal disease, the mortality and morbidity of the procedure must be borne in mind. As in the case of other new methods this will depend to a considerable extent upon the proper selection of cases and on the skill of the individual operator. It need hardly be said that he should not embark on the procedure without proper instruction, but even so disasters can occur.

I have personally observed one case of lumbar aortography in which the needle entered through an atheromatous plaque, resulting in tearing of the aorta with the subsequent death of the patient. Dos Santos reports only one death in over 3000 lumbar aortographies. This was due to the tip of the needle being introduced through the cœliac axis into the superior mesenteric artery. Injection of the contrast medium resulted in gangrene of the small intestine.

The number of cases of malposition of the needle which one has seen makes it surprising that the mortality is not higher than it is.

There is no doubt that the injection of a large amount or of a high concentration of the contrast medium into the kidneys results in severe tubular damage and anuria. Fortunately, in many cases these changes are reversible, but it is of the greatest importance to inject only the minimal amount to give a diagnosis. Whilst the retrograde method with the Seldinger or Odman catheter has been relatively free from the complications of the lumbar technique, nevertheless there have been cases of thrombosis of the femoral artery.

PERCUTANEOUS PUNCTURE OF RENAL CYSTS

As has already been indicated the differential diagnosis of renal neoplasms may be difficult or impossible by means of urography or pyelography. It is true that aortography will usually provide the answer, but another simpler and safer method has been described by Lindblom (1946). This consists of localizing the lesion on the fluorescent screen after retrograde pyelography. A needle is then passed through the skin of the back to a predetermined depth. If a cyst is present the fluid comes out readily. A small quantity of contrast medium is then inserted and a radiograph taken. In the case of a cyst within a tumour the difference in the size of the cyst and the tumour will be apparent. It is our custom to aspirate these cysts, as reaccumulation of fluid appears to take place rather slowly. If Lindblom is unable to aspirate fluid from the kidney, he injects a small quantity of contrast medium which he claims produces a characteristic pattern in cases of hypernephroma. On account of the danger of disseminating the cancer cells, we have hesitated to use this method.

PERIRENAL INSUFFLATION

This procedure is used mainly in the examination of the suprarenal glands, but is also of value in demonstrating the size and shape of the kidneys when for some reason aortography is contraindicated. The best method is to insert a needle through the sacro-coccygeal joint into the pre-sacral fascia. About one litre of oxygen is then injected slowly, and in about thirty minutes it has ascended into the perirenal fascia. Plain radiographs, or preferably

tomographs, will then generally give a clear outline of the kidneys and suprarenals.

EXAMINATION DURING OPERATIONS

Not infrequently the surgeon has difficulty in finding a renal calculus demonstrated in the plain radiograph. In such cases a film in a sterilizable flexible cassette can be placed in the wound behind the kidney and the exposure made with a mobile x-ray apparatus. By using a highly active developer and fixer the wet film can be viewed in the theatre in $1\frac{1}{2}$ to 2 minutes. This not only shows the position of the calculus, but may also demonstrate others whose presence was unsuspected. Various methods of fluoroscopic demonstration of calculi at operation have been described but the danger of x-ray exposure to the theatre staff renders this a hazardous procedure.

IMAGE INTENSIFICATION AND CINERADIOGRAPHY

In many hospitals retrograde pyelography is carried out under fluoroscopic control. This ensures adequate filling and prevents overfilling, but little detail can be seen in the calyces. Fluoroscopy has been used in excretion urography and some observers claim to have observed normal peristalsis and filling defects in the calyces. Detail, however, is so poor that Braasch (Braasch and Emmett, 1951) has pointed out that the technique is bound to be inaccurate and leaves much to the imagination. In recent years an electronic method of intensifying the brightness of the fluoroscopic image has been developed. By means of the image intensifier it is possible to carry out fluoroscopy with a tube current of between one-third and one-fifth of that normally used, thus diminishing the x-ray dose to the patient and observers by the same order. At the same time the image is so bright that much detail is visible in the renal pelvis, calyces and ureters, even in excretion urography. I have found it possible to carry out retrograde pyelography with subdued room lighting and useful information can also be obtained in excretion urography (Stevenson, 1957). It is a simple matter to fix a ciné-camera to the intensifier, and by this means secure a permanent record of the calyceal and pelvic movements. This has been found particularly useful in renal tuberculosis and obstructions at the pelvi-ureteric junction.

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ORTHOPÆDIC CONDITIONS ASSOCIATED WITH CHILDBEARING

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Minor anomalies of the skeletal system, which are normally compensated for, may be brought to light by pregnancy. Postural defects, in particular, may be accentuated and, for the first time, give rise to symptoms. During pregnancy diminution of muscle tone, softening and relaxation of ligaments and altered body mechanics may make the primary trouble worse, and the symptoms may not improve later because involution of the muscles and ligaments has been delayed due to inadequate rest after the birth of the baby.

UPPER LIMB PAINS

Acroparæsthesia.—In this condition the patient complains of numbness, tingling and pain in the hand. The middle three fingers are most commonly affected and may show some diminution of sensation to pin-prick and cotton-wool. The pain may radiate more widely up the forearm. Symptoms are worse towards the end of the day and in bed. Relief is obtained by rest and by elevation of the shoulder, a fact which the patient discovers for herself by sleeping with her arms above her head. The discomfort is usually unilateral and affects the dominant hand.

The condition is a variant of the thoracic outlet syndrome in which there is abnormal pressure on the neurovascular bundle in the region of the first rib.

Such pressure has been attributed to cervical ribs and bands from the tips of rudimentary cervical ribs, a posterior insertion of scalenus anterior, a band passing under the bundle from the scalenus anterior to the scalenus medius, undue obliquity of the first rib, bands in Sibson's fascia over the dome of the pleura, post-fixation of the brachial plexus and nipping of the axillary artery by the two heads of the median nerve.

X-rays rarely show the presence of a cervical rib in the acroparæsthesia of pregnancy, and the other anomalies cannot be diagnosed clinically. Moreover, these anomalies are rare, whilst acroparæsthesia is quite common.

It is believed that the symptoms in pregnancy are due to stretching of the normal neurovascular bundle over the normal first rib. This may be explained by the relatively horizontal position of the first rib occasioned by the change to costal breathing in pregnancy and by the relative weakness of the trapezius muscle which allows the whole shoulder girdle to sink downwards. This is confirmed by x-rays which show the approach of the clavicle to the first rib, as compared with the non-pregnant state. This hypothesis is supported by the facts of the general muscular weakness of pregnancy, the x-ray findings, the relief of symptoms by elevation of the shoulder and by

the restoration of tone in the shoulder-girdle muscles, and by the disappearance of symptoms in the puerperium.

Since the disorder is self-limiting the aim is to make the patient more comfortable. Rest achieves this object and may be reinforced by the use of a sling arranged to lift up the point of the elbow and so the shoulder. Exercises to restore the tone of the trapezius and other muscles of the shoulder will also help. Most patients will be quite unable to devote time to the relief of their symptoms, and are quite happy to put up with their discomfort. They need only be reassured that neither they nor their babies will suffer any harm, and that the condition will disappear shortly after labour.

The carpal tunnel compression syndrome is not often seen in pregnancy. The symptoms are very similar to those of acroparæsthesia; some believe that the thoracic outlet syndrome is very rare and that nearly all cases are in reality due to compression of the median nerve in the carpal tunnel. The discomfort may radiate widely up the forearm, as in acroparæsthesia. Since the palmar branch of the median nerve passes superficial to the flexor retinaculum, sensation in the middle of the palm is not diminished.

Relief of the symptoms is obtained by splinting the wrist, with the joint in the mid-position or slight flexion. An extension plaster may stretch the nerve. In the non-pregnant state, division of the flexor retinaculum is sometimes required, but rarely should this be necessary in pregnancy. If one accepts the diagnosis at all in pregnancy it may be that the nerve is œdematous, perhaps because of hormone changes causing water retention, and the œdema might be expected to diminish in the puerperium. Therefore the decision for or against operation should wait until after the baby is born.

Subscapular pain may be complained of when the baby is a few months old. The dominant side is affected and it will be found that the baby is always carried on this arm. By using her other arm more, the patient can cure herself.

CHEST WALL PAINS

Cough fracture of a rib is not uncommon in the later months of pregnancy. A violent cough swings the lower ribs inwards where they come up against the resistance of the fundus of the uterus. In these circumstances a rib may fracture. The 9th and 10th ribs are the ones most often broken, and usually on the right side where the liver increases the resistance to the sudden movement of the ribs. The patient complains of the sudden onset of pain during a bout of coughing. Palpation will discover a tender area on the rib. X-rays demonstrate the fracture, but it may have to be looked for very carefully since it is often only a hairline crack.

As this is a fracture due to muscular violence it is obvious that instead of a bony injury muscle fibres may rupture. The clinical picture is then the same except that the x-rays show the ribs to be intact. Rarely a pleural rub develops at the site of the fracture hæmatoma, and some patients may have pneumonia prior to the fracture or develop it subsequently when the pain limits chest movement.

Treatment depends upon the severity of the pain. Analgesics and strapping the chest are mainly employed. The strapping should be applied from above downwards, with the chest in expiration. Rather more than half the chest wall should be encircled and a generous overlap above and below the fracture should be allowed. If the skin is painted with Friar's balsam before the plaster is applied, irritation is much reduced. The strapping can be removed at any time if the patient is uncomfortable with it. It is valueless in helping the fracture to heal and is only justified by the relief of symptoms.

Interchondral subluxation is occasionally seen. When the woman bends down, the fundus levers up the lower costal cartilages so that the 9th rides over the 8th or the 8th over the 7th, so straining the small joints between them. The history is clear-cut, the patient having a sharp pain at the site of subluxation on bending. As she straightens up the subluxation reduces itself, but soreness persists. The site of the pain may be found by palpation, and pressure on the upper costal cartilage reproduces the pain. X-rays are, of course, no help in this cartilaginous area. The rectus abdominis muscle is attached to the 5th, 6th and 7th costal cartilages and overlies these interchondral joints. Pain in this area has often been ascribed to rupture of a few muscle fibres. In the type of case just mentioned muscule rupture is very unlikely since the rectus abdominis is not contracting during trunk flexion. Because the liver increases the leverage on the lower cartilages, this painful condition is most commonly seen on the right side.

Treatment is not usually necessary, the patient being advised not to bend down. If the discomfort is severe, infra-red therapy will help.

BACKACHE

This may be complained of in any part of the back, but only lumbar, lumbo-sacral and sacro-iliac pain, together with coccydynia will be considered here. The symptoms occur in later pregnancy and for some months after the puerperium. During the lying-in period the woman has adequate rest in bed and so rarely has backache.

Nearly all the backaches of childbearing are postural in origin. One can pick out the women who will probably have backache as they walk into the antenatal clinic. They will often wear high-heeled shoes. The abdomen and pelvis are thrust forward and the shoulders carried well back increasing the lumbar lordosis. The smock hanging from the shoulders tends to obscure the lordosis, but the collar does not fit the back of the neck, because the neck is slightly flexed to compensate for the 'swayback'. One has only to stand for a moment or two with the lumbar spine in extreme lordosis to feel the kind of discomfort which many pregnant women have.

The small joints between the articular processes of the vertebræ are probably the site of the pain. In lordosis they are at the extreme of their range of movement. Any joint kept at such an extreme will cause discomfort. The pivot of movement between adjacent vertebræ is situated just behind the mid-point of the intervertebral disc, so that the ligaments behind this will be slack and therefore unlikely to be the source of backache, when the back is fully extended.

The typical history of a postural backache is that there is some discomfort on rising but this goes quite soon with activity. It returns during the late morning when the woman has been bending over the sink, making beds and polishing floors. It is relieved by sitting down but not for long, unless she makes quite sure that the lumbar lordosis is eliminated. Towards evening the ache returns and is relieved again by sitting down, only to return if she sits still too long. In bed the pain is relieved but has returned by early morning. The patient soon realizes that to obtain maximum comfort she must arrange her day with periods of rest and activity.

During the puerperium backache is rarely complained of. The woman is resting and her thoughts are directed to the baby. A month or two after the birth, however, backache is common. In pregnancy there is relaxation of the ligaments of the pelvis and lumbar spine, together with a decrease in muscle tone and altered posture. After the birth, time is necessary to allow involution of ligaments, and restoration of tone and posture. The time necessary varies in different women and postural reflexes laid down in pregnancy may be difficult to discard. This is particularly so when the woman has to return to a household where there are other children whom she must care for, and where the new baby is such a drain on her energy and time. There is more work at the sink and in bending over the infant in its cot or bath; the work increases as the child gets older, heavier and more active. While the backache is at its worst the 'periods' are often irregular and heavy. It is not surprising therefore that the woman believes she has some pelvic abnormality causing both symptoms. In the past, doctors, too, have agreed with their patients so that retroversion and cervical erosion, both of which may be physiological, have quite wrongly been blamed for causing backache. It needs to be emphasized that nearly all backache arises in the back.

The diagnosis of postural backache is not usually difficult. The history is the greatest help. If the pain has the time relationships suggested above, and if there is no doubt that the ache is worse on bending, walking and polishing and like activities, the symptom must be skeletal and not pelvic, no matter what pelvic abnormalities are found. The patient is asked to demonstrate the site of pain. This is usually done with the back of the hand and the localization is not precise. If the pain is in the lumbar area the cause is not genital. The four main sites of postural backache are the lumbo-sacral joint, the sacro-iliac joints and the sacro-coccygeal joint. The ordinary active movements of the spine will be full so other methods must be used.

The woman lies flat on her face. Firm pressure with the 'heel' of the hand is made on the sacro-iliac joints in turn and then on the lumbo-sacral area and the lumbar spines. Pressure at one or other of these places will often reproduce the pain and one then knows it is skeletal. Holding one hand firmly on the sacrum each hip is then forcibly hyperextended. This pulls on the ilio-femoral ligament of Bigelow, thus rotating the half pelvis and straining the sacro-iliac joint. Quite often this will reproduce a mild abdominal pain and it is common to find sacro-iliac pain referred anteriorly.

Next, with the arm beneath both thighs and the other hand pressing on the

lumbo-sacral area the pelvis is lifted off the couch and the lumbar spine fully hyperextended. This action will reproduce lumbo-sacral backache. Forced rotation is done with the patient on her side. The pelvis is pushed one way and the shoulder the other, and this should be done in both directions.

With the patient on her back each hip is fully flexed and the knee pressed on to try to rotate the sacro-iliac joints, and finally both knees are pressed on with the hips flexed to test flexion of the lumbar spine and lumbo-sacral joints.

Finally the tendon reflexes are tested, the sciatic nerve stretched by Lasègue's manœuvre and an x-ray of the appropriate area taken. A pelvic examination is obviously also necessary. In postural backache there will be no x-ray, neurological or pelvic findings of abnormality. Too much reliance has been placed on radiography and for an exact diagnosis it must be possible to reproduce the symptom by appropriate manipulation of the back. During pregnancy full manipulative measures of diagnosis cannot be applied and x-rays should not be taken. One must then be content with the history and pressure in various areas to make the diagnosis. But with the patient on her side the lumbar spine can be hyperextended and strain put on the sacro-iliac joints, so clarifying the diagnosis.

Coccydynia may often be the cause of an obscure backache. The pain from the area may spread widely and have many characteristics of a postural backache, but it may be accurately localized to the coccygeal region. In all doubtful cases the coccyx should be firmly pressed on when the patient is on her side and if the finger is put in the rectum the coccyx is easily manipulated to reproduce the pain.

TREATMENT OF BACKACHE

Treatment in pregnancy is often not necessary and not wanted by the patient. If she can be reassured that the backache is due to the altered posture of pregnancy and that neither she nor the baby will be harmed she will usually be content. Analgesics may be prescribed and she herself will find a judicious mixture of rest and activity which will keep her symptom bearable. Some sacro-iliac strains are very severe and may necessitate complete rest in bed. Others, not so severe, are helped by a course of short-wave diathermy and gentle exercises about three times weekly for a month or six weeks.

Palliation of coccydynia is achieved by rubbing in liniment of methyl salicylate two or three times daily. If this is not enough, short-wave diathermy is of value.

When postural backache occurs after the birth of the baby, rest and relief from work are the best treatment, but often they cannot be applied. It is then necessary to use short-wave diathermy and exercises directed to postural re-training. Sometimes a surgical corset or Goldthwait brace may be necessary but these should not be used until a fair trial of physiotherapy has been made.

PROLAPSED INTERVERTEBRAL DISC

This diagnosis is made much too often in connexion with childbearing. Postural backache is much commoner, though, of course, disc lesions do

occur. If a backache arises in pregnancy it is well not to accept a disc etiology unless there is an acute onset on straining or definite sciatica. Pain in the buttock does not constitute sciatica and is most often referred from the sacro-iliac joint. A diminished ankle jerk and positive Lasègue's sign confirm the diagnosis of herniation of a disc. Treatment is on the same lines as in the non-pregnant patient. When necessary a brace can perfectly well be worn in pregnancy.

When a disc lesion has occurred before pregnancy the woman is very prone to exacerbation of her backache. Treatment may be continued as necessary through pregnancy, but the main necessity is adequate rest. In labour, flexion of the spine should be avoided. It is perfectly possible to conduct the whole of the second stage with the patient in the left lateral position. Forceps delivery, too, may be carried out with the woman in this position, or, failing this, helpers may hold the legs in the lithotomy position, so that the back is not flexed.

Rarely a disc protrusion may have been of such severity before pregnancy and been so difficult to cure that the orthopædic surgeon's advice should be sought. He may feel that Cæsarean section will carry less risk of recurrence of prolapse of the disc than vaginal delivery. If the spine has been grafted the indication for abdominal delivery may be greater.

TUBERCULOSIS OF THE SPINE

In the acute phase this is rarely seen in pregnancy. Even in the healed phase it is uncommon. In all such cases an orthopædic surgeon's advice should be sought. The main worry in pregnancy is whether backache is due to recrudescence of the disease, and this often cannot be decided till after pregnancy. Fortunately, most backaches in the healed tuberculous spine are of postural origin. In such spines there is some rigidity caused by the fusion of bones, either naturally or operatively. The rigidity is often compensated by undue mobility elsewhere in the spine, and the backache is at the site of compensation rather than at the primarily diseased area.

Treatment is primarily by rest and this must obviously be more rigidly enforced than in the patient with a healthy spine. Care of the back in labour is very necessary and sometimes the risk of flaring up the disease is best minimized by Cæsarean section.

CONGENITAL ANOMALIES OF THE LUMBAR SPINE

These are rarely diagnosed except by x-rays and with the diminishing use of radiography in pregnancy will not often be diagnosed then, for rarely is a backache in pregnancy of sufficient severity to warrant an x-ray of the lumbar spine. A few months after the baby is born a persistent backache will require an x-ray for full diagnosis. Even though this shows lumbarization of a sacral vertebra or sacralization of a lumbar vertebra or any of the other anomalies in this area, it must not be assumed that backache is due to the congenital defect. Quite often a clinical examination in the manner previously

suggested will show the pain arising in some different site. It may be that rigidity or mobility bestowed on the lumbo-sacral region by the anomaly is compensated elsewhere in the lumbar spine and that the compensating area is the seat of the backache. In such cases an orthopædic surgeon's advice should be sought.

PELVIC OSTEOARTHROPATHY

During pregnancy the ligaments of the pelvis soften and relax allowing some mobility at the pubic symphysis and the sacro-iliac joints. In some women the relaxation is of such degree that movement is excessive and causes pain. The woman complains of pain in the lower abdomen on walking. Pressure on the symphysis reproduces the discomfort and so does pressure on the anterior superior iliac spines in an effort to separate the two halves of the pelvis. Sometimes with the patient standing on each foot in turn the pubic bones may be felt to ride up and down. Occasionally the pain of pelvic osteoarthropathy comes on for the first time in the puerperium. An x-ray will show undue separation at the symphysis but, as the radiological gap in the normal pelvis is quite large, the interpretation of the film needs some care. Since the pelvis is normally a firm osseo-fibrous ring it is obvious that if the symphysis separates there must also be laxity posteriorly. This is found in the sacro-iliac joints, which in such cases are often the seat of pain.

The best *treatment* is rest; sometimes the symptoms are so severe that the woman has to take to her bed. Relief can be obtained by winding a 6-inch (15 cm.) flannel bandage round the patient just below the iliac crests in an effort to close up the pelvis. This is better than using adhesive plaster since the woman can remove the bandage at will. In the puerperium a counterbalanced canvas sling will help to approximate the two halves of the pelvis when pain is severe. In the milder cases activity should be graded and rest must be insisted upon to allow involution of the ligaments. If this is not done she may have a chronic legacy of sacro-iliac backache.

MULTIFIDUS SYNDROME

In this disorder tender nodules may be found in the area of origin of the sacrospinalis over the back of the sacrum. On superficial examination it may be confused with sacro-iliac strain. Treatment is by injection of procaine and 'hyalase' into the nodules.

LOWER LIMB PAINS

Pain in front of the hip is commonly complained of in pregnancy. Its cause is probably the stretching of structures anterior to the joint. With the lordosis of pregnancy there is often some degree of pelvic rotation; also, when the pelvis is thrust forwards in advance of the plane of the ankle joints, the hip joints are kept at the extreme of extension. Relief from pain is obtained on sitting, and otherwise the woman needs only reassurance.

Meralgia paræsthetica is a complaint in which numbness, tingling or pain may occur in the distribution of the lateral femoral cutaneous nerve. There

is dullness of sensation in the middle third of the outer side of the thigh. Symptoms are not usually severe and improve or disappear in the puerperium. Sometimes residual disability persists. The cause of the symptoms may be pressure on the nerve roots by a prolapsed disc or on the nerve where it splits the inguinal ligament, which it does in some people, or in the tunnel for the nerve in the fascia lata.

Treatment may be by the rubbing in of methyl salicylate liniment in the mild cases. In severe cases rest may be necessary. If symptoms persist beyond the puerperium a neurologist's advice should be sought. Sometimes surgery is advised to free the nerve from pressure at the inguinal ligament.

Flat feet tend to be made worse in pregnancy for obvious reasons. Treatment by the use of appropriate footwear and exercises is valuable, for flat feet may be responsible for multiple postural adjustments in the knees, hips and spine all of which may be the site of pain, whilst the feet are overlooked.

THE PUERPERIUM

Most of the disorders previously considered clear up or improve in the puerperium, mainly because of the rest obtained, but also because muscle tone and better posture are restored. Moreover, the elation of childbirth pushes the more mundane matters of minor aches and pains into the background. But there are two sequels of labour to be considered.

Fracture of the coccyx and coccydynia may occur as a result of normal labour, but more commonly are seen following forceps delivery. The pain may radiate from its primary site of origin, so the diagnosis is made by manipulating the coccyx, which reproduces the discomfort. Classically, of course, the pain is worse on sitting and defæcation. *Treatment* consists of infra-red or short-wave diathermy and analgesics in the first instance. If the pain persists other measures may be necessary and are best left to the orthopædic surgeon.

Foot-drop is not common in the puerperium. It may follow normal or instrumental delivery and is caused by interference with the function of the lateral popliteal nerve. There is weakness or paralysis of the dorsiflexors of the foot and numbness or paræsthesia on the outer side of the foot. Pressure on the nerve may be by an acute prolapse of an intervertebral disc or directly by the forceps or fœtal head in the pelvis. Some would add the pressure of the lithotomy pole where the nerve winds round the neck of the fibula, but this seems unlikely. Sometimes the leg may 'jump' during a forceps delivery and this may herald the onset of the foot-drop. Traction on the nerve, acute disc prolapse or pressure in the pelvis may all perhaps be responsible at different times. Early recognition is essential to reap the greatest benefits from treatment. An orthopædic surgeon should be consulted.

The main lines of *treatment* are: (a) adequate splinting to prevent stretching of weak or paralysed muscles, (b) active exercises to maintain tone in the muscles, (c) full passive movements of the affected joints twice daily to prevent contracture and particularly equinus deformity, (d) massage and

faradism to maintain tone. Later a toe spring with an inside iron and outside T-strap may be of value when the patient is ambulant. Treatment may be necessary for up to two years, for although sensory recovery is usually complete motor weakness may persist.

AFTER THE PUERPERIUM

In the few months following the birth of the baby the commonest skeletal complaint is of backache. A careful history will often show that this began in pregnancy. It is usually of the postural type already described and should be investigated in the same way. At this time an x-ray should be taken to exclude other causes, but in the postural backache it will be of no help. Moreover, active movements are usually full and only forced passive movements will reveal the site of origin of the pain. Because the periods are often irregular shortly after childbirth there is a tendency to look for a pelvic cause for backache. It is this tendency which has caused the quite undeserved reputations of retroversion and chronic cervicitis.

MISCELLANEOUS CONDITIONS

Rheumatoid arthritis tends to improve in pregnancy because of the increased secretion of cortisone.

Acute poliomyelitis in pregnancy is treated without reference to the pregnancy. The first stage of labour may be conducted with the patient in a respirator and so may the second and third stages. An intratracheal anæsthetic is safe if instrumental or operative delivery is necessary, and the patient has to be taken out of the iron lung. If respiratory distress is evident in the second stage an episiotomy and low forceps delivery under local anæsthesia is ideal. *Abdominal muscle paralysis* after poliomyelitis usually causes no trouble in labour. Occasionally forceps delivery for inadequate expulsive power in the second stage is necessary.

In paraplegia the labour may be painless if the lesion is above the 10th thoracic segment. The second stage may be prolonged because of inadequate sensation and expulsion. Forceps should then be used.

Fractures in pregnancy are uncommon, but it should be borne in mind that eclamptic fits may cause fractures of vertebræ and the humerus, as well as other bones.

SUMMARY

Many aches and pains associated with childbearing are due to faulty posture, because of altered body mechanics and diminution of muscle tone. The site of the pain may be determined by strain falling on a previously existing abnormality whether this be congenital or acquired. The skeleton developed evolutionarily for quadrupedal progression. The upright posture puts such a skeleton at a disadvantage, which is accentuated by the mechanical and hormone adjustments of childbearing.

THE ART OF ANÆSTHETIZING CHILDREN

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'Non ignara mali miseris succurrere disco'.
'Not unschooled in woe do I learn to succour unhappiness'.—Virgil.

In 1957, over 200,000 children were admitted to hospital for tonsillectomy in Britain: this represents two-thirds of all admissions of children to hospital in this country. The art of anæsthetizing children is not an easy one. Specialists in pædiatric anæsthesia are justly proud of the way in which modern techniques are used to facilitate a pleasant 'going to sleep' effect with a minimum of psychogenic and physiological disturbance, but not every doctor called upon to give an anæsthetic to a child has at hand the technical skill or the material facilities necessary to obtain the best results. The method to be described enables the user to render a better service to the child, with the minimum of aid.

ESSENTIAL PREREQUISITES

Normally preoperative medication is given with the intention of minimizing the body reactions to fear and anxiety: reducing the secretions of the salivary glands and the upper respiratory tract, and lowering the basal metabolic rate. This latter purpose is of particular importance in pædiatric anæsthesia. Often, however, the intended effects of the premedication are not achieved because of faulty timing of administration or inequality of effect upon the patient. Ideally, the child should reach the operating-theatre environment in a state of reasonable quietude, non-apprehensive, and with the minimum of mucus in a clear respiratory tract. If, however, the timing is not right or if the sedation is ineffective the child is alerted towards fear —with consequent hyperadrenalinæmia.

Guedel (1937) suggested that the important factor of an increase in the basal metabolic rate producing a degree of resistance to the induction of anæsthesia could be varied by several factors, all largely controllable by the anæsthetist. The basal metabolic rate varies, with peaks in early school age and at the onset of puberty. Factors influencing anæsthesia in the child are the degree of reflex irritability and the rate of consumption of oxygen based upon the energy requirements of the child. Guedel stresses that the level of the metabolic rate is important when considering the starting point of induction of inhalational anæsthesia. The immediate pre-anæsthetic metabolic rate is influenced particularly by the presence or absence of fever, pain, and emotional excitement. In many cases of operation in childhood the presence of fever and pain must be accepted by the anæsthetist. They

may be the results of conditions necessitating the child being brought to operation. The anæsthetist therefore, realizing that they will raise the effective metabolic rate, does his best to minimize this by controlling the degree of emotional excitement that is present.

This third factor can be regarded as the commonest and the most important factor in the production of a raised metabolic rate immediately preceding the start of anæsthesia: for to bring a child into an operating theatre is to disturb him. The child has been removed from his own familiar environment, from his mother: he is surrounded by unfamiliar faces; these people are all *busy* in a way uncomprehended by him. The child's world is egocentric—he is disturbed and frightened by the unfamiliarity of it all. Again, the anæsthetist is aware of the summation of effect of all these factors piling as it were Ossa on Pelion.

Of the five senses, hearing is the last to be overtaken and suppressed by inhalational anæsthesia; as the patient passes under the influence of the anæsthetic sounds become enormously magnified and distorted. Nothing is more frightening than to feel that one has lost the power to move or cry out, yet at the same time to be overwhelmed by tremendously loud noises, culminating in hearing someone roar: 'Can I start now?' or 'It's all right, you can start now'.

THE STAGES OF ANÆSTHESIA

The effects of inhalational anæsthesia have been divided into four 'stages', but only two need be considered here. In stage I, that of analgesia, the patient passes from consciousness to unconsciousness; during it the sense of pain is removed before the sense of touch. Concurrently with the loss of pain there is a relative loosening of control by the higher centres. Continuing, the patient loses consciousness and passes into stage II, that of delirium, in which control by the higher centres is lost completely. Nervous response to external stimuli and dreaming is increased, and may be expressed in the form of physical activity. During passage through stage II the sense of hearing remains longest, and so physical violence (i.e. uncoordinated sudden violent movement of the patient) is often initiated and even potentiated by sudden noise. Moving of the patient or too early an attempt to carry out surgical toilet on the table may also induce undesirable movement. Particularly important to the anæsthetist should be the realization of the danger of permitting the patient to hear talk about the impending operation. Babcock (1944), discussing excitement in anæsthesia, observes that the patient is unconscious but delirious; any painful stimulus brings on active muscular response. Holding of the breath is common, due to laryngospasm, and hence anoxia and even cyanosis result.

A patient who is frightened and struggles during the first stage can present a more dangerous and difficult anæsthetic problem than the patient with an easy induction.

McDowall (1952), investigating the deleterious effects of anoxia, has shown that it can exert a slow, insidious, and delayed effect, through disturbance of the electro-

lytic balance in the tissues between the inside and outside of cells. Normally, the cell membrane is relatively impermeable to the passage of sodium ions inwards, the 'sodium pump', as it is termed, pushing sodium out from the tissue cells into the inter-cellular fluid and plasma. Oxygen lack, by rendering the cell membrane more permeable, allows sodium and chloride ions to enter, thus disturbing the electrolytic balance. Once this happens the excitability of the tissues is altered. This has been shown particularly in the case of nerve tissue, striped and cardiac muscle tissue.

Evans (1954) considers that when the patient is excited or struggling it is often difficult to achieve a sufficient concentration of ether vapour: recurring periods of such excitement lower the vitality, and lengthen the postoperative recovery of the patient. In brief, the greater the amount of fear (which is not always obvious to the anæsthetist) the greater the likelihood of marked physical disturbance in stage II. Once the physical activity has appeared the second stage is usually prolonged.

The spectacle of the struggling child undergoing induction requires consideration. The effect on the child can be imagined. He recovers from the nightmare of such an induction only to find himself in pain. It has been said that the child is father to the man. One has often wondered at the extent of the amount of iatrogenically induced fear that may result from such handling. As Ostlere (1953) significantly remarks:—

'Many patients paradoxically are more afraid today of the anæsthetic than of the operation they are about to have, due to memories of "suffocation" when as a child undergoing their first operation'.

Curran and Guttman (1943), discussing the etiology of mental disorder, state that it must be clearly recognized that the demands made by the environment are never in themselves the cause of mental disorder, but that environmental stresses act indirectly only by virtue of the emotions they produce. Shakespeare was indeed a good psychiatrist when he made Mark Anthony say: 'The evil that men do lives after them'.

Study of the literature has shown that these views are in accord with those given by many pædiatric anæsthetists of great experience and authority. The techniques described by them are of great interest and help to those concerned with the problem of anæsthetizing children (Beecher, 1938; Haglund, 1952; Heerdegen and Attwood, 1954; Hewer and Lee, 1957; Kepes *et al.*, 1955; Lundy, 1943; Macintosh and Bannister, 1947; Ostlere, 1953; Westhead, 1951; Woolmer, 1953). In certain important aspects, however, no attention is paid to the actual problem of the doctor, who may be a less experienced anæsthetist, faced with the need to anæsthetize a child.

A SIMPLE TECHNIQUE

With these considerations in mind I wish to describe a technique which is simple and effective, requiring the aid of only one other person, which demands of the anæsthetist only quietness and gentleness, and which aims at reducing the physiological and psychological trauma of inhalational anæsthesia in children to the absolute minimum.

When the child arrives in the anæsthetic room immediately preceding induction, silence from all present is the rule. It is unfortunately all too

common for nurses who are necessarily busy to be rather noisy at times, with consequent frightening of the child, premedicated though he may be. It is clearly understood that the anæsthetist is the only one who speaks to the child. In a laudable desire to help, well-meaning attendants by their untimed and possibly inapposite interruptions often make matters worse.

Before speaking to the child a quick glance at the case-sheet confirms his name: his first name only is used. Children are egocentric; when spoken to in a manner suggesting they are known as individuals they respond well. The child is never asked a question; he is always *told* what is going to happen in the most matter of fact tone of voice. In this way he is shown that it is natural for him to do what he has been told to do. Children respond most readily to such leadership—the anæsthetist must always be in command of the situation. In simple language I tell the child, who is now lying supine, to bring his hands up together on his chest, just under his chin, and to clasp them together with the fingers interlocked ('like this'—showing and guiding him at the same time as I talk to him). Once accomplished, this is the *first essential, effective and simple step*—the only one to be carried out by the patient.

The ward nurse stands on the child's left side. She is asked to place her right hand gently over the child's clasped hands: in this way she can most effectively control movement without exerting undue pressure. She then places her left hand across the child's knees (which are under the blanket) with equal gentleness and firmness, exercising control over lower limb movements when needed. If left-handed, the nurse must stand on the child's right side: the important factor is that control of the child's hands must be by the nurse's master hand. She has already been told that she must not let the child's clasped hands escape from her grasp, or the knees to become flexed, and that she must be attentive to every potential movement the child makes while he is being anæsthetized. As soon as she senses incipient movement she should exert just sufficient counter-pressure to maintain the child's limbs in position. On no account must she let go of the child's clasped hands. Provided that the nature of exercising preventive control by increasing the counter-pressure necessary just to hold the hands and knees in place has been fully explained and equally fully understood, anyone can give this effective help. This is the *second essential, effective and simple step*—the only one to be carried out by the assistant.

I now talk to the child quietly and start the inhalational anæsthesia. (The anæsthetist should always use the particular technique most suitable in the circumstances of facilities and climate, and which he has found most effective in children.) While the child passes through stages I and II, absolute silence is maintained. On entering stage II, the patient is unable to move very much. When struggling, while being anæsthetized, the first step is to move the hands up towards the face so as to push away the offending mask. With the hands clasped together and the fingers interlocked, movement of the fingers in an attempt to disengage them only causes them to

lock more firmly in position; control by the attendant nurse is thus easily maintained.

In this way directly by gentle pressure on the head when holding the face-piece (or open mask) in position, and indirectly through control by the nurse, the anæsthetist is able to exert a three-point method of physical fixation of the patient. With gentle firmness and in silence he can thus take the patient through stage II with considerable rapidity into stage III, and on to the plane required for the operation. When muscle tone has been abolished, the nurse is told to release her gentle grasp.

Using this method there is but little if any struggling or any undue heightening of tension; the environmental silence is more than golden; physical stimuli are prevented or severely limited. The anæsthetist may, for example, find it wiser not even to alter the position of his hand holding on the mask or face-piece throughout induction; only when the patient is in stage III should he insert the air-way. It should be regarded as a confession of failure if any child who has been anæsthetized, using this technique, is taken from the anæsthetic room into the theatre with the hands not still clasped gently together on the upper chest wall, in the position in which they were originally placed.

SUMMARY

A case has been argued for the use of a simple technique to be applied to children undergoing inhalational anæsthesia with the purpose of enabling anæsthetists to produce much good with little ill. It is gratifying to note the rapidity and ease with which a child can be anæsthetized in this manner. During the past decade a succession of junior hospital residents have welcomed the demonstration of this technique which by its simplicity and effectiveness gives so much confidence to the less experienced anæsthetist. General practitioners to whom this technique has been demonstrated have also expressed their appreciation of its value. A further valuable factor is the feasibility of application anywhere in the world where a doctor (who may be an inexperienced or occasional anæsthetist) is called upon to anæsthetize a child.

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THE FIRST SYMPTOM

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It is an insult to the most developed animal system on this planet, the human nervous system, to suppose that the first symptom of any disease is not a mental one. That an invasion by micro-organisms can take place on the frontiers, that errors of absorption should allow some foreigner to circulate in our sovereign realm, that the scales of hormonal balance should wobble, or that cell proliferation—that ancient protective mechanism that accounts for anything from a corn to a cancer—should begin to pile up without the imperial mind reacting in some way seems to me to be biological treason.

Even pain from sudden trauma is preceded, if only momentarily, by the panic of shock, but in most of the assaults on, and diseases of, mankind pain is a late symptom; subtle changes have occurred in the mind long before clamant pain. Here, in caricature, is an illustrative case. A man with an incipient corn, long before it reaches consciousness as pain, will, because of it, take a bus where previously he walked, will avoid as uncongenial the hearty Brown who at week-ends does his thirty miles and boasts about it only by meiosis, will find that literature like 'With Hillary on the Heights' or 'Tramps in Togoland' is mildly repellent, but enjoy Miss Austen, and find himself again taking an interest in his youthful pursuit of philately. This is a functional reaction which may prevent the corn and constitutes the first symptom of a corn. Generally it is disregarded and a corn forms. If it is something more serious, say heart disease, the first symptoms are more likely to persist and consolidate; one recalls that Lord Northcliffe with his endocarditis proclaimed that games and exercise were waste of energy.

For hundreds of years it has been noticed that a sense of well-being precedes an attack of gout, but the well-being is of a particular kind, a full-barns feeling with the testiness of power and much meanness in it, which in reality is due to the mobilizing of urates *et al.* in the blood. In the regression of alcohol something like this phase is passed through just before the generous phase, when even the poorest of us scatter largesse in thought; the two are distinct but parallel places on specific tracts on the broad highway of regression. In practice I have found that similar but distinctive expansiveness precedes an attack of fibrositis. One recalls many an indignant moan like this: 'He comes home after his work, mows the lawn, has his tea, then he mows the neighbour's lawn and cleans out the fowl-house, then he sits in his damp clothes going through some old papers till eleven, and now he's surprised he's got his lumbago again'. What probably happened was something like this. A spell of sedentary life and good living had caused quite a number and variety of metabolites to circulate in the blood stream;

the good dog, Histamine, whose function it is to protect the purity of the protoplasm, had herded many of them into the intercellular spaces and here they had accumulated, especially in the intercellular spaces of the large buffering muscles. Now metabolites act as mental stimulants ('A writer should not be in too exuberant health', writes Eric Linklater in 'A Year of Space'; 'I can't write a line', said Morley Roberts, 'if I am in robust health'), but metabolites in muscle cause that particular kind of mental stimulus which results in exercise, the primal object of the mental stimulus being to remove those metabolites by exercise. One small irrelevant bye-point—the reason why the fibrositis tends to recur at intervals in the same place and pattern is that the intercellular spaces have been established and enlarged and remain in being like empty bladders, albeit microscopic. Lumbago's wife was confusing the first symptom with the cause: and she is not the only one as many a psychiatric paper shows. In nine cases out of ten the first symptom which is essentially protective will ward off the disease, but when it fails to do so, even by the learned it will be indicted as the cause.

REGRESSION

When the adventurous amœba, pushing out its pseudopodia of desire, comes into a patch of poisoned water or other danger, it resumes its spherical form and thereby for a minute or so cancels its commitments and presents a smaller and less vulnerable target. If some astral naturalist visited this planet, that, I think, is the first habit he would notice in man: his dignified reception committee of personages are like that only for a very short time; they regress in eating and drinking, in their homes, quickly with alcohol and with stress and emotional conditions; there is an almost total regression even unto the amœba itself in sleep; man is in a state of flux, ever ready to obey Nature's 'As you were'. But it is the regression in illness that concerns us here and I suggest that the first symptom is invariably in the mode of thought, that it is probably different for each disease or each type of disease, and that it must long precede any of the grosser changes like heightened temperature or quickened pulse or any alteration in behaviour.

But before we spot any alteration in the thought process we must have some idea what is the normal.

FORMS OF CONSCIOUS THOUGHT

Few people analyse their streams of consciousness and in no two people would the forms of consciousness be in the same proportions. This briefest of summaries begins with the most specialized minds and applies to the time when they are not regressed.

Professorial types think in ideas and concepts with a few seen or heard word labels. They have lost their power of visual thinking and of introspection. This applies to men only; scholastic women, however erudite, always retain a modicum of sensory thinking.

Ordinary adults: a jumble of picture-thinking which is slightly coloured and indistinct, imaginary conversations and monologues, concepts and ideas, and very occasional smell and touch thoughts.

Adolescents: childhood fantasies are becoming practicable. Many bundles of sensory thoughts, scenes, sounds, tastes, and experiences, first, second and third hand are being tied up into ideas and concepts, generally with a sensory or emotional label. Coloured picture-thinking which is losing its vividness and heard word-thinking which is losing its hallucinatory clearness predominate.

Late childhood: the time of the functional fantasy, the blue-print of desire, chiefly mechanical now. Vivid coloured picture-thinking which is slow moving predominates. Ideas and concepts can easily be broken down to their sensory components. Heard word-thinking is in short sentences and ejaculations. Taste, smell and touch thoughts are being curbed, but alimentary, muscle and joint thoughts stimulate the fantasies.

Younger children: highly coloured picture-thinking predominates, often of close-ups; heard words are just captions and often rhyming and metrical; taste, smell, touch, alimentary, muscle and joint thoughts are insistent. The motifs of the fantasies are amœbic in the sense that they push out in adventure and pull in for security. In the former there is an uncritical sense of wonder. Adults in the regression of dreams can see the Archbishop of Canterbury blithely riding a hippopotamus in the Grand National, with wonder but without the slightest sense of incongruity—until they awake.

It is an alteration in this motley stream from the sovereign mind, always a regression, that we must look for as the first symptom of any disease.

ALCOHOL

Evidence of the stream of consciousness and its regression in illness depends upon skilled questioning and on introspection; obscure and unconvincing stuff especially to the educated person whose currency of thought is mainly in concepts and ideas. But a path of regression, a finger-posted path, can be demonstrated in himself and to his friends if even the most erudite male takes a sufficiency of alcohol. This primrose path has been sketched in a little book on alcohol, published by the Medical Research Council, in oft-quoted words:

> '. . . it is in short a narcotic drug . . . always a lowering of functional activity . . . the main effects of alcohol that have any real significance are due to its action on the nervous system . . . a sense of careless well-being and bodily and mental comfort. . . . Alcohol successively weakens and suspends the hierarchy of functions of the brain, and therefore of the mind, in order from above downwards, that is to say in the inverse order of their development in the individual and the race . . . and thus it facilitates escape from reality and from feelings of weariness, encouraging day-dreaming, wish-fulfilment and a general regression towards the earlier and more primitive levels of childhood and infancy'.

That sounds as if it were written on the morning after; the joyousness, the matiness, the giving vein, the sense of adventure alternating with a

dream of security, the wide-eyed wonder are forgotten. Nor is the alcoholic path of regression which leads to sleep a sleepy one; when passing through the adolescent stage our guinea-pig, our alcoholic professor, is distinctly liable to pranks as every magistrate knows, and to song and dance. Somewhere below this level is the stage where rhyming and clanging noises are so attractive and emotions and facts are expressed in metrical sounds and half-suggesting words, the poets' level. One remembers Lord Tennyson's bottle of port a day, and that, according to Haydon, once for six weeks Keats was hardly ever sober. Good taste forbids instancing more modern poets. But Keats also had tuberculosis and that has its own path of regression; he mixed his toxins with a vengeance and left us memorable emotions in the amber of words. Morphia also has its peculiarly attractive path of regression, as Coleridge and de Quincey found to their cost.

Meanwhile we are not straying from our subject: The First Symptom; our thesis is that the stream of consciousness is the most delicate gauge of health and any disease or poisoning will show itself first by causing a regression in the mode of thought. It is the only way the mind can act in adversity, but the paths of regression are many and specific. Pains and aches, alterations in behaviour, speedy E.S.R.'s and whatnot will come later, but this is the first symptom, and until we know what is the normal we cannot recognize regressions from it. That is to say, it is by introspection that we spot the first symptom—which may do its job and avert the disease—and by direct leading questions of the intelligent.

THE COMMON COLD

Those of us who are trained in watching our own mental activities, who are introspective in this sense, are like most of humanity very limited in our personal experience of disease. I do not know what are the subtle mental changes which accompany the onset of diabetes, hypertension, uræmia or carcinoma; I could guess at them from the parallels of the diseases that I do know and from the fact that there is always a functional urge in the change; I would guess, for instance, that the fantasies that precede hypertension have the bustle of business in them and that these, amœbically, alternate with dreams of tranquillity; I guess, but I do not know.

Like most, I do occasionally suffer from that viral invasion which is called 'a common cold'. Hours before the first sneeze, which itself is hours before the feel of battle for the nasopharynx, I get certain mental changes: familiar places, an office or a sitting-room becomes dreary and loathsome and has a smell about it, which is a child's and savage's way of labelling localities; familiar faces assume the Hogarthian touch, strange, of the earth earthy and rather repellent, memories of the open air, rugger and the sailing of small boats, whiffs of woodland, moor and fen present themselves, and the habit of fantasy, almost purposefully forgotten in most adults, comes back and weaves around these subjects. Nature is saying, wisely or unwisely, 'Go for a five-mile walk, man!'. Later come the fantasies which depict a

paradise of warmth and solitude where one would be, but, if one can obey them, before long the vivid coloured adventure fantasies come back and urge. Much later, when the bacteria and cocci have joined in the fight, their poisonous and thought-restricting action makes the picture confused. Robert Graves wrote of his 'flu' in 'Good-bye to all that': 'My temperature was running high now and my mind was working clearly as it always does in fever. My visual imagery, which is cloudy and partial at ordinary times, became defined and complete'.

Even that amount of volunteered insight is rare, but dozens of people have been asked about this and those who are intelligent enough to understand and introspect have given a great variety of answers with broad similarities, and in most the utilitarian hand of function is apparent. My point is that before a cold could even be a suspicion of a cold there are changes in that most delicate gauge, the stream of consciousness.

TUBERCULOSIS

There is one disease of which I have had ample experience; I have been apprenticed to the *Mycobacterium tuberculosis* for forty-two years, a capricious master. He always makes his presence known by giving a vivid sensorial form of thinking, the first stride of regression. In 1915, at Frimley Sanatorium for three months every day at about 2 p.m. he gave me most exciting fantasies of the blatantly egotistical kind—Hollywood's worst. They lasted till 2 a.m. when down came the damp curtain of a night sweat. While they lasted they were so enthralling that even the interruption of meals was resented. And they had the power of a suggestion given to the hypnotized; they were insistent, indeed compelling long afterwards. 'Go round the world', ordered M. T., and months later I went round twice in thirteen months. 'There are some names that intrigue me', said M. T., 'Esmaralderes and Shimonosekei, let's go and have a look at them'. So we went. 'There's trouble at Murmansk—or Chanak—or in the Far East, we ought to have a glance at that'. So we trailed off, again and again. 'But we haven't been round the Horn', said M. T. Well, one's not a sailor until one's been round the Horn, so we packed up again and went off, but we never saw it because we had to go too far south to avoid ice.

A characteristic of M. T. is that he will lie low for years, apparently asleep, and then suddenly disturb a stolid and sedate elderly gent. by giving him adolescent fantasies. Sometimes, however, he leaks continually, hence the legion of tuberculous novelists. I feel sure that he lurked in an ischio-rectal abscess in Charles Dickens, a profitable combine like the mycorhizal association with the root-hairs of trees. The Battle of the Giant Cells can go on for years—for a lifetime—without ever giving rise to overt tuberculosis. There are many other causes of regression, but this is the one which most often accounts for the inexplicable little tragedy: the hard-working and hard-playing boy who suddenly flops in his work and his games, the clean-living curate whose restraint goes and who commits a sex crime, the

bank manager who is a churchwarden and suddenly starts embezzling, the extraordinary error of judgment in the judicial, the pricked bubble of a rising reputation, examples of all of which have been within my experience.

In my own case M. T. has had bouts of leaking. In 1929, even before the stitches came out from a thoracoplasty he made the most invigorating suggestion that we should go back to the sailing of small boats, giving fantasies which brought with them the feel of the tiller, the sounds of the sea and the complex smell of a cabin. This resulted in the purchase of *Louise*, a half-ton cutter. We started off in a gale and ran on a mud-bank, but lived in intermittent and nautical sin for a year, when she was jilted for another. M. T. always makes his presence known by giving these adolescent fantasies: that is to say, they are among the first symptoms. He is not a deep regressor, he does not take one back to early childhood as alcohol can. Mark the broadly functional nature of an adolescent return, fewer commitments, healthier surroundings, a more vigorous endocrinal defence. It is also worth noticing that the fresh wind of a tactless adolescent approach has its uses in a dug-in urbanized society.

Wakley of *The Lancet*, for instance, who fought nepotism, privilege and restrictive practices in our own profession. There is need of many Wakleys today when leadership has been sold for secret pieces of silver, when a qualified man is debarred from practising in many parts of his own country, and State practices are awarded by nepotism or worse. Wakley showed his tuberculosis for the first time in his sixties, as did Sir Arthur Keith, though of course the battle of the giant cells had been going on most of their lives. This elderly tuberculosis is becoming important now and has been attributed to smoking. Far more likely it is due to a waning endocrinal protection which amongst other things mediates the adolescent fantasy and provides the first symptom.

THE PSYCHOSES

Freud wrote: '. . . that so many things that in the neuroses have to be laboriously fetched up from the depths are found in the psychoses upon the surface, visible to every eye'. This is certainly true in the matter of the regression of thought giving rise to the first symptoms of a psychosis. It is also to be expected because the psychoses are in the main primary or genetic regressions and not usually secondary, in peace time at any rate, to somatic assaults.

A matron of a private mental hospital had a list of the first signs that her cyclothymic patients were about to enter the manic phase: Mrs. X would put on a black silk dress, Miss Y would ask for a third cup of tea, Miss Z would beseech the doctor for a cigarette, and so on. But these are physical signs, the fantasies of grandeur, expansiveness and matiness which gave rise to them had been building up for weeks. Standing with the medical superintendent in a room and idly watching through the window the patients on parole going out we saw one of them walk across an oval of grass instead of walking round it like the others. The M. S. rang the bell

for an attendant: 'Send someone to fetch Mr. Blank, he's just gone out, and he's not well'. But Mr. Blank got to far-away London. For how long had some fantasies of liberty and fleshpots been forming in his mind, the hidden first symptoms?

It is only as a naturalist that one ventures to speak about this most specialized of all specialties, a naturalist with his obsession for function. A busy barrister who had been casually accused of stealing an umbrella told me that for weeks afterwards his mind was occupied in delivering histrionic defences of his action, a slight regression to the heard-word mode of thinking, the sort of retreat which when the restraints go gives rise to paranoia. The regression in schizophrenia to adolescent and childhood fantasies and the contrast between these and their come-backs to normality, which has given rise to the 'schizo' idea; the tidality of cyclothymia which must have been of great advantage to us when we were brutes of the foreshore; the return to childhood in senility with its simpler wants and renovated memories of a child's state, all of these show the utilitarian hand of function and indicate where we may look for the first symptoms.

PSYCHOSOMATIC DISEASE

That the hyperæmic patch near the pylorus should, minute by minute, worry the mind and make it give persistent pictures of food or dreams of asceticism, the first symptoms, and that very occasionally when this is not effective the cunning mind after months of nagging should use this as an excuse for putting off a visit of a mother-in-law, and that in consequence of this an ulcer should develop as it has no protecting fantasies, is only to be expected and with a few million variants has given rise to the psychosomatologists. They may be regarded as penitents who, or whose forbears, fell into the Heresy of Departmentalism and are now returning to the faith of the early fathers: Sydenham and Harvey and beyond even unto the holoistic Plato.

SUMMARY

This essay lays it down as an axiom that the first symptom of any disease must be a mental one. It gives some evidence from the diseases personally known to the writer. That other diseases, rheumatoid arthritis, for instance, or malignant disease, with their vast cellular changes, their hormonal panics and the touch of death in them are long preceded by changes in the delicate stream of thought, which can be altered by mere tiredness: to deny this seems stupid—the transparent stupidity of a deaf man who pretends he can hear. I do not know what these changes are, but they will be tracks on the broad highway of regression and will exhibit a blind effort to avert the evil, to function.

No graphs or statistics are offered; the evidence which comes from a host of leading questions and introspection is shadowy, not substantial stuff, like the glories of our Church and State. In short this is a speculative essay, of little practical use, hardly worth reading. But fun to write.

FAMILY PLANNING

By L. N. JACKSON, *M.C.*, D.M.
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ACCORDING to the 1957 'Demographic Year Book', published by the United Nations, world population in 1956 was estimated to be about 2,737 million. More than half of these do not get enough to eat. Every year world population increases by 1.6 per cent. which means, in round terms, an annual increment of 40 million more mouths clamouring to be fed.

THE PROBLEM

Viewed objectively, this spectacular increase in human numbers is the most challenging phenomenon in this century of alarums and excursions; much more so than the hydrogen bomb.

What has brought it about? Not a sudden and inexplicable increase in human fecundity which, broadly speaking, varies but little. It is the direct consequence of the triumphs of modern medicine. Pandemics and epidemics of once mortal maladies no longer rage. Endemic diseases, such as malaria, are fast disappearing from the face of the earth. Through improvements in hygiene, and in preventive and clinical medicine, fewer and fewer of those born die untimely deaths. In a word, death has been controlled.

So much for the credit side of the account; but there is also a debit side. Survival has little value if it means merely an insecure foothold, a precarious clinging to life with no prospect other than that of starvation or near-starvation, which is the lot of many in the world today and will be of more tomorrow. It may be argued—and, indeed, is argued—that all that is necessary is to apply modern scientific methods to agriculture on a world-wide scale and all can become well fed. The expert answer to this is that whereas food supplies can, at best, be increased only by *arithmetical* progression, population is increasing by *geometrical* progression. Improvements in agricultural techniques and production are more than offset by population increase, and the gap widens. It is further argued that migration can provide the answer, but countries have grown selective about their immigrants and vast hinterlands awaiting development no longer exist. In any event, migration can prove only a temporary expedient. Unless we are 'to leave it to nature'—and that means to famine—to balance population and food production, it is obvious that action must be taken, and quickly, on a world-wide scale. Yet the World Health Organization, which is so largely responsible for death control, has so far virtually ignored the necessary corollary of birth control. This, briefly, is the case for family planning as an instrument of human welfare.

WHAT IS BEING DONE

Certain governments in Asia have recognized the peril of over-population

and are taking vigorous measures to combat it. The Japanese Government, faced with the problem of a population rapidly approaching the 100 million mark and with no possibility of increasing agricultural acreage, has not only launched an extensive programme of family planning but has also, as a desperate resort, legalized abortion and popularized sterilization. The Government of India, as part of its second Five-Year Plan, has intensified its earlier efforts to control that country's population of more than 357 million by the establishment of numerous urban and rural family planning clinics, by financial help to State Governments and to voluntary bodies to be used for similar purposes, and by the extension of training facilities. The Government of Republican China, responsible for 630 million persons increasing annually by at least 12 million, has grasped the importance of family planning. Free contraceptive advice is available at clinics in all large industrial centres and is being taken to the rural areas.

Elsewhere the situation varies considerably from country to country. In the United Kingdom family planning, largely through the pioneering efforts of the Family Planning Association (FPA) but without any government support, has come to be accepted as a necessary service. The FPA services now comprise 270 branch clinics in England, Scotland and Wales, of which 25 are new ones started in the past year, during which a total of one-third of a million people have been helped. Although the FPA receives some financial and other help from local authorities and regional boards the prospect of an Exchequer grant is as remote as ever and its activities depend largely upon private subscription. The FPA concerns itself not only with family planning in both its negative and positive aspects: it is interested also in marriage guidance, sponsors literature and has recently received a grant of £30,000 to be used in the search for a simpler contraceptive.

In the United States the situation is less satisfactory. Although widely established as a voluntary service organized under the Planned Parenthood Federation of America, family planning receives no government support and is still illegal in two of the States and sometimes classed with pornography. In the U.S.S.R., although it would be contrary to Marxist doctrine to advocate the limitation of population on economic grounds, there is evidence of an increasing awareness of the need for contraception as a means of safeguarding maternal health and of combating abortion. A scientific committee is being organized there which will concern itself largely with research in the field of contraception and the establishment of contraceptive centres. The Scandinavian countries have extensive and well-established family planning services and, on a less developed scale, the same applies to much of Western Europe. The movement is gaining a foothold in various countries of Africa but Central and South America remain virtually untouched.

INTERNATIONAL COOPERATION

The International Planned Parenthood Federation (IPPF) came into being in 1952 with three main objectives: the formation of family planning

associations in all countries; the training of doctors, nurses, health visitors and social workers in the practical administration of family planning services; and the encouragement of research into human reproductive processes and into biological methods of controlling fertility. Its headquarters, at 69 Eccleston Square, London, S.W.1, acts as an information centre on the population and family planning problems of all countries. Books, journals, films and speakers are available on request. Thanks to the generous cooperation of the FPA of Great Britain, training courses in family-planning techniques are arranged for doctors, nurses, health visitors and social workers. The IPPF has member-organizations in twenty-two countries and territories: Australia, Barbados, Belgium, Bermuda, Ceylon, Denmark, Great Britain, Holland, Hong Kong, India, Italy, Jamaica, Japan, New Zealand, Pakistan, Puerto Rico, Singapore, Sweden, Switzerland (Canton de Vaud), Union of South Africa, U.S.A., and Western Germany.

The IPPF organizes international and regional conferences. The third regional conference recently took place in Jamaica and the sixth international conference will be held in Delhi next year. An international news bulletin appears ten times a year in English, Flemish, French, German, Italian and Spanish editions, and the IPPF issues each year a directory listing family planning agencies all over the world.

SOME RESEARCH PROBLEMS

At the IPPF Regional Conference held in Jamaica last April only moderate satisfaction was expressed with regard to existing methods of contraception by the combined use of mechanical devices and chemical preparations of various kinds. These are regarded by most workers in this field as too elaborate and expensive for widespread use among less developed communities. In the United States there is a move towards single, chemical methods and in various parts of the world efforts to find better methods, especially oral ones, are in full swing. Among these may be mentioned the work of Dr. S. N. Sanyal, of the Calcutta Bacteriological Institute, with extracts derived from the common pea (*pisum sativum*); of Dr. M. C. Shelesnyak, of the Weizmann Institute of Science, Rehovoth, Israel, who, experimenting with rats, is attempting to elucidate the mechanism of the implantation of the blastocyst and is able, by the injection of ergotoxine, to prevent it; and of Dr. J. B. Thiersch, of the Department of Pharmacology of the University of Washington, who is working on the control of reproduction by the use of antimetabolites. Perhaps the most promising research is that being undertaken in Puerto Rico by Dr. Gregory Pincus, Research Director of the Worcester Foundation for Experimental Biology, and Dr. John Rock of the Harvard Medical School, working with a group of 19-*nor*-steroids which, taken orally, inhibit ovulation. In the Oliver Bird lecture delivered on April 9, this year, before the Society for the Study of Fertility, Dr. Pincus reported the results of a two-year clinical trial of one of these compounds carried out in 125 women. Among those who took their medica-

tion regularly over two years no pregnancies occurred. This result is undoubtedly impressive but many years of observation are needed to ensure that these compounds produce no long-term ill-effects.

Even when a cheap, harmless and reliable 'pill' has been discovered there will remain the problem of what in America is called motivation: the difficulty of getting the pill accepted and used by women on a world-wide scale in the face of apathy on the one hand and of an unbridled maternal impulse on the other.

THE CHURCH AND FAMILY PLANNING

Family planning is actively supported, or at least passively accepted, by most of the great organized religions of the world. It is approved by all Christian denominations except the Roman Catholic Church which sanctions no methods of birth control other than those of sexual abstinence and the observance of the so-called 'safe period'.

At the Church of England Lambeth Conference in 1930 contraception was held to be permissible among married persons by a three to one majority. The 1958 Conference has given consideration to a report entitled 'The Family in Contemporary Society' published by the Society for Promoting Christian Knowledge. This report summarizes the views of a group of sociologists, theologians and demographers convened by the Church of England Moral Welfare Council at the behest of the Archbishop of Canterbury, under the chairmanship of Canon M. A. C. Warren, general secretary of the Church Missionary Society. This group, the report states, finds 'nothing Christian in the suggestion that the so-called "natural checks" (of disease, war and abortion) should be left to exercise their own restraint on population'. If governments consider that it is their duty to encourage family planning, the group 'cannot say that Christians ought to withhold support'.

THE G.P. AND FAMILY PLANNING

What, at the present time, should be the general practitioner's function with regard to family planning? Assuming that he sees and accepts the urgent need for it, he would be well advised to take a short course of training to familiarize himself with the simple techniques of contraception. He would then be in a position to offer a family-planning service to his own patients without their having to attend a clinic often many miles distant at considerable personal inconvenience. If he is not prepared to do that, he should at least take the initiative in advising his married women patients to attend the nearest clinic without waiting to be asked. An obvious opportunity to do this as a routine presents itself on the occasion of the post-natal examination when the doctor can point out to the post-partum patient the manifest advantages of spacing the births of her children. Nor should the general practitioner neglect the positive side of family planning: the not uncommon case of the couple who ardently desire a baby and cannot get one. Such couples, not the wife alone, should be referred to clinics for the investigation and treatment of their infertility.

GENERAL PRACTITIONERS' FORUM

THE USES OF HYPNOTHERAPY IN GENERAL PRACTICE

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Hypnotherapy has had a chequered career, and even at the present time is not widely accepted as an ethical procedure. It is often said, particularly by the layman, that he 'does not believe in it', in the sense that he does not believe that the phenomenon exists. For good or ill, however, it does exist, and, even more incredible to the lay mind, it requires no special skill, so far as induction goes.

INTRODUCTION

The reasons for the widespread distrust of hypnotism are due in part to its widespread use by showmen and charlatans for purely commercial ends, but also to the lack of scientific knowledge concerning the hypnotic state. Recently, however, hypnotherapy has become more respectable. Public concern at the dangers of stage performance, led to the passing of the Hypnotism Act (1952), which forbids 'an exhibition, demonstration, or performance of hypnotism on any living person at, or in connection with, an entertainment to which the public are admitted'. The first prosecution was brought under the Act in April 1954 (*Manchester Guardian*, 1954).

During the last four years also there has been no lack of attention to the matter in journals often seen by the general medical reader. In 1954, the *Lancet*, reporting the work of Kitching (1953) set out the indications and dangers, in addition to an outline of method. In 1955, the Report of the B.M.A. Subcommittee on Hypnosis was published and commented upon (*Brit. med. J.*, 1955). This report places hypnotherapy firmly within the province of psychiatry, but recommends that 'medical undergraduates be given a description of the possibilities, limitations, and dangers' and also 'that instruction in the clinical use be given to postgraduates training as specialists in psychological medicine, and possibly, anæsthetics'. The report also recalled the statement of a previous B.M.A. committee in 1892 that 'hypnotism is frequently effective in relieving pain, procuring sleep, and alleviating many functional ailments'. A report by the French Royal Academy of Science came to similar conclusions in 1831. Other recent reports of an optimistic nature are those of Asher (1956), Goldie (1956), and Brown (1956).

In these reports there is little indication of the possibilities and difficulties that might be peculiar to the application of hypnosis in general practice. The present article is a review of some of these and a report of the first nine cases on whom hypnotherapy was attempted, under the conditions of everyday general practice under the National Health Service.

METHODS

First attempts at hypnotic induction are an alarming but exciting experience. Despite the present-day acceptance of hypnotherapy, there is a strong

feeling that one is departing from the realms of medicine, to the extra-terrestrial atmosphere of parapsychology. There is an uncomfortable feeling that failure of induction will be embarrassing, but that success will lead to a situation analogous to that of the sorcerer's apprentice. In fact, complete failure to induce at the first attempt has been known to deter altogether from further attempts. The basis of success and confidence is undoubtedly selection of cases, and personal experience of this is more impressive than the literature. One special difficulty from the general practitioner's point of view is the necessity for the presence of a chaperone when dealing with female patients. A sympathetic relative, however, has been found to be most helpful in this respect, and reassuring to both doctor and patient. Some diffidence was often felt in suggesting this form of treatment. To some extent a patient who is referred to a special clinic for treatment is conditioned to what he is about to undergo, but a suggestion from his family doctor of an unusual form of treatment may cause surprise and uncertainty. The doctor-patient relationship here is a unique one, and the practitioner himself may consider that he is jeopardizing that intimate and trusting condition which is so valued on both sides. Experience has shown, however, that, in the right cases, this need be no bar to hypnotherapy and indeed may often be turned to advantage.

The method described by Asher was the one used. Following the suggestion that hypnotherapy be tried, an appointment was made, and at least fifteen minutes set aside for the session. The patient lay on the surgery couch, in ordinary lighting, and was asked to concentrate his gaze on the end of the therapist's pen which, held about four feet (120 cm.) away, in the patient's line of vision, was slowly rotated. The patient was then persuaded to relax and was told in a monotonous voice that he was beginning to feel sleepy, and that his eyelids would soon begin to close. This was continued until the patient was drowsy and unable to open his eyelids.

With regard to susceptibility to this form of hypnosis, the figures quoted by Kitching are: 90 per cent. will feel drowsy and comfortable, without actually falling into a hypnotic sleep, 10 to 40 per cent. will enter a state of deep hypnosis, and less than 10 per cent. will go into a hypnotic coma. These figures were borne out in the present series of patients, who were seen during the period June 1956 to June 1957.

CASE RECORDS

Case 1.—A housewife, aged 62, with agitated depression. For three months she had been complaining of insomnia, loss of appetite, and fullness after food. The previous history was uneventful. She had been investigated at the local hospital and the report was that there was no evidence of organic disease. An acute exacerbation of agitation and foreboding that 'something terrible was about to happen to her' led to an urgent message for a visit late one evening. Attempts to calm her being of no avail, it was decided, with the relatives' consent, and in their presence, to attempt to induce a hypnotic sleep. This was immediately successful, the patient going into a light trance, muttering the Lord's Prayer as she did so (as this was the therapist's first experience of hypnotic induction, his uneasy feeling that he was allied to the Forces of Evil was thereby enhanced!). At this and two further sessions held at the surgery,

suggestions that she would lose her phobias and feel happier, were of no avail, and she was soon after admitted to a mental hospital. She remained there for three months undergoing electroconvulsive therapy, and has since remained well.

Case 2.—A male machinist, aged 46, with primary obsessional neurosis. For over 15 years this patient had been troubled by vague uneasiness and gastro-intestinal discomfort, fear of crossing bridges, and feelings of impending death. On one occasion he refused dental treatment lest he should die under the anæsthetic. He had been repeatedly investigated by physicians, surgeons, social workers and psychiatrists, who blamed, respectively, over-smoking, a deflected nasal septum, overcrowded living conditions, and coitus interruptus. In 1955, he was admitted to a mental hospital for electroconvulsive therapy, and was discharged slightly improved, with a prescription for amylobarbitone ½ grain (30 mg.) twice daily. His symptoms having returned, the patient readily agreed to a trial of hypnosis. Four attempts at induction failed, however, in spite of the utmost willingness on the patient's behalf, and treatment with sedatives was therefore resumed.

Case 3.—A male, aged 40, who was a display artist, requested reference to a hypnotherapist, as he was smoking 60 cigarettes daily, and had been unsuccessful in his attempts either to reduce his consumption or to stop altogether. He agreed to hypnosis being attempted at the surgery, and on the third induction a light plane of hypnotic trance was achieved. Suggestions were then made that he would find smoking distasteful and be able to overcome the desire to smoke. With each session his consumption decreased until, by the eighth, he had reduced his smoking to 12 cigarettes daily, but he was unable to stop smoking altogether. Two months later he reported that he was smoking no more than 15 daily, but six months later this had increased to 30. In this patient it was found possible to demonstrate post-hypnotic amnesia, by the usual methods: e.g. at the suggestion of the therapist he would on waking 'forget' the number '6', and count 'one, two, three, four, five, seven', etc.

Case 4.—A female, aged 23, a factory hand, was an example of acute hysteria in an unstable personality. In response to an urgent call this single girl was found apparently in status asthmaticus, a condition she had often witnessed in her mother. The patient herself had never suffered from respiratory trouble of any sort. Her past history included tonsillectomy, trichomonas vaginalis infestation, incomplete abortion, and appendicectomy after numerous false alarms. A normal appendix was removed on that occasion. She had also been seen, more recently, at the surgery, complaining in a short space of time of pruritus, urticaria, and headache. On the present occasion, no abnormal physical signs could be detected, and a diagnosis of hysterical overbreathing was made. It transpired that the patient had just returned home after a few days' absence, and a family dispute had arisen. This had been curtailed by the onset of her symptoms. Hypnosis was thereupon undertaken at the bedside. The patient rapidly responded to suggestions that her breathing was returning to normal, and her hypnotic drowsiness merged into normal sleep. She awoke next morning perfectly well.

Case 5.—A schoolboy, aged 11, with bronchial asthma. This was the typical asthma of childhood, partly infective in origin and partly nervous. Having been called out to an acute attack, which was accompanied in the usual way by anxiety, I first gave him adrenaline, 10 minims (0.6 ml.) subcutaneously. Bearing the previous case in mind, he was then asked to close his eyes, and with the light subdued, he was subjected to repeated suggestions that he was going off to sleep, and that his dyspnœa was easing. He soon went off to sleep, and did not wake until morning.

Case 6.—A female schoolteacher, aged 25, had suffered from childhood from a coarse tremor of both hands—at times of stress only. Repeated neurological investigation had always been 'negative', and her symptoms had never been influenced. She agreed to a trial of hypnotherapy, and a light plane of trance was achieved with ease. The suggestion that she would be able to control her nervous trembling, and be less nervous in company, was made repeatedly. There was never the slightest sign of any improvement, and after eight attempts, the treatment was abandoned,

and she was once more referred to a nervous diseases hospital, which was also unable to help her.

Case 7.—A housewife, aged 50, with involutional depression. She complained of repeated short attacks of depression, much worse since the menopause two years previously. At that time she had received supportive treatment from a psychiatrist, and had since taken sedatives and œstrogens. On the present occasion, she was first referred to a day hospital where she received electroconvulsive therapy as an out-patient. There was a temporary improvement for a while, but she then returned complaining of recurrence of depression, and was continually troubled by the thought of suicide. She refused further electroconvulsive therapy, and 'supportive therapy' was started at the surgery: i.e. weekly or twice-weekly talks at which she was allowed to air her problems, and at which encouragement was given. As no progress was made, hypnotherapy was suggested and the patient agreed. After three sessions, however, in which light hypnosis was achieved, she declared that she felt ashamed of being hypnotized, and confessed that she thought of other things while she was supposed to be asleep! Therapy was therefore discontinued. She continued to call in at the surgery, however, for a chat with the receptionist on several occasions, and subsequently improved.

Case 8.—A housewife, aged 58, had an anxiety neurosis. She had had neurotic symptoms for many years, and had been taking thyroid for six months (for hypothyroidism), when she had an acute hysterical screaming attack, which led to a call late at night. Hypnotic induction was attempted but the patient was totally unresponsive. Morphine, ¼ grain (16 mg.) intramuscularly, rapidly achieved what hypnosis had failed to do.

Case 9.—A housewife, aged 47, had an anxiety state with hysteria. She has 27 letters in her file, mainly from gynæcological registrars driven to desperation. One letter ends: 'I advise hysterectomy, as I feel that one woman's womb matters less than one doctor's life'. Two years previously she had been an inpatient at a mental hospital, and since her discharge had spent most of her time in bed, neglecting her housework and her family. Her family history was poor: her father had hanged himself, when the patient was 5 years old. The future history of her own child seemed to be in jeopardy, as he ran away from home on one occasion with his dog, in order to escape from the dreadful life at home. On the present occasion, as the situation was deteriorating, she was referred to a day hospital. Here she settled down for a week or two, with occupational therapy. She soon had an argument with the therapist, however, refused to attend any longer, and resorted to her bed, and her gynæcological symptoms. The husband agreed to a trial of hypnosis, as an alternative to readmission to a mental hospital. The first induction was at the bedside, and on eight subsequent occasions at the surgery. She improved rapidly, and responded to suggestions that she would stop worrying about her neighbours, that there was no physical disease of her internal organs, and that she would lose her desire to stay in bed, and be able to get on with household duties. The last session was in July 1957, and the patient has not relapsed. Although it is difficult to believe that the improvement will be long lasting, this case must be considered a success, so far.

DISCUSSION

Nine patients were selected for hypnotherapy in the course of one year's work in a medium-sized National Health Service practice. In view of the experimental approach and the results obtained, it would seem, on the whole, that this form of treatment might be used with benefit on less than half a dozen occasions in a year in the average general practice, and the question arises whether this is sufficient for a reasonable degree of proficiency to be achieved or maintained. Of the nine cases selected, two (cases 2 and 8) failed to show any change in their level of consciousness. Of the others, benefit was obtained in five cases, but there was no useful result in two

(cases 6 and 7). That acute hysteria responds to hypnotherapy was borne out by case 4, and, although other methods of treatment exist, it is believed that hypnosis can be more rapid and more easily applied than, for example, persuasion and explanation, or psychotherapy. Acute hysteria, in the frank form presenting here, however, is not very common in general practice.

The results in the case of over-smoking are encouraging, and have often been demonstrated. Cases such as this raise fundamental questions on the mechanism of hypnosis, and the alteration (albeit temporary) in the personality, leading to achievements of which the unaided will is incapable.

From the remaining three cases two useful principles emerge. That hypnotherapy has a place in general practice as a means of calming patients who suffer from either an outburst of excitement or an overlay of anxiety, in conjunction with a more serious underlying disease, is clearly demonstrated in cases 1 and 5. It may well be asked, however, whether in these circumstances hypnotic induction is any better than more conventional sedatives. This question remains open, but it is felt that there is a useful tool here, for the general practitioner to be aware of. Case 5 in particular illustrates very well the way in which the knowledge of the powers of suggestion may be adapted to allay anxiety and produce sleep in a restless patient. There is little doubt that sleep was produced here in a more satisfactory way than if a sedative had been given. There is nothing new, of course, in this approach, which is merely an extension of the idea of a good 'bedside manner'. It is quite analogous to the common way in which children's fears of a dental anæsthetic are overcome by soothing and soporific murmurs from the inducer.

With regard to case 9, a second important point of discussion arises. Whilst bearing in mind the fallacies and dangers of deducing a general rule from a single case, it cannot be denied that hypnotherapy was followed by a great improvement in this patient's condition. It is true that the change in her mental state may have been spontaneous, as so often occurs, and it is doubtful even whether the change will be more than temporary. Nevertheless it seems probable, from the gradual improvement that occurred with each session, and from her previously long-continued ill health, that hypnotic suggestion played some part in the return to mental health. This being so, there is some indication here of an additional therapeutic tool for the treatment of the difficult psychiatric case by the general practitioner. The danger is of transference or dependence to such a degree that an untrained therapist may find himself in an embarrassing position, and the patient be left, in the words of Brown (1956), 'nursing the chronic resentment of the half-seduced'. This is one of the most often stressed dangers of hypnotherapy undertaken by an untrained person.

This case also illustrates an all too common difficulty. Faced with a difficult case of neurosis, the general practitioner is often at a loss to know what to do. He is faced with the alternatives of referring the patient to the psychiatric outpatient department, where there is a long waiting list, and

where, because there are too many patients for too few doctors, treatment is sometimes, from necessity, perfunctory, or seeking to obtain admission for his patient to a mental hospital. This, unfortunately, is still tainted by stigmatization, and again prompt admission is not always possible. Few patients are able to afford admission to private mental homes. Of outside help, the most useful has been found to be the day hospital. Here, patients in need of urgent attention can get it, and without the unfortunate social consequences of being 'sent away' even voluntarily. Outpatient electroconvulsive therapy, weekly (or even daily) psychotherapy, and occupational therapy are often very successful in rehabilitating the patient, with a minimum of disturbance of family life. Unfortunately, however, day hospitals are not widely available and, as case 9 illustrates, not always successful in helping the patient. What then is left to the general practitioner, apart from asking his patient to leave his 'list', and go somewhere else? Psychotherapy by the patient's own doctor must be the answer and if in this event he 'rushes in, where angels (in this case, psychiatrists) fear to tread', he must be aware of the possible dangers of so doing. Nevertheless, it is felt that there is a place for psychotherapy in general, and hypnotherapy in particular, in the management of neurosis, in his surgery or at the bedside, by the general practitioner. Perhaps it should be stressed again that one case is not enough from which to draw general conclusions; on the other hand it is quite sufficient to awaken one to perhaps useful possibilities.

SUMMARY

Hypnotherapy was undertaken in nine selected patients during the course of one year's general practice.

Induction failed in two cases, and two more were not influenced by the treatment.

A case of over-smoking treated by hypnosis is reported.

From the remainder, two tentative conclusions are drawn. First, that the principle of suggestion may be useful in general practice in allaying anxiety, and in inducing sleep. Secondly, that in difficult cases of neurosis hypnotherapy by the patient's general practitioner may occasionally be of value, notwithstanding the dangers of psychiatric complications.

I would like to acknowledge that interest in the uses of hypnosis in general practice was aroused by a demonstration given by Dr. Richard Asher at the Willesden general hospital in 1956.

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A DIAGNOSTIC PROBLEM

By W. M. CHESNEY, *M.C.*, M.B., B.Ch.
Birmingham

A man, aged 60 years, complained of pain in his right foot when walking. The pain appeared to be located in the transverse arch and in his outer toes, and was elicited by weight-bearing, the onset being immediate when his weight was borne on the forepart of his foot. Simultaneously there was a definite plantar flexion spasm or active clawing of the three outer toes. The other findings were: flattening of the metatarsal arch, palpable foot pulses, a blood pressure of 140/95 mm. Hg and a urine free from albumin and sugar.

A POT-POURRI OF CONSULTANTS

For the next two years he attended hospitals more or less regularly, and during that period was examined and treated by four consultant surgeons (three orthopædic, and one interested in peripheral vascular disease). The various diagnostic labels were peripheral vascular disease, peripheral vascular spasm, metatarsal planus, and weakness of the lumbrical muscles allowing the toes to claw. Therapies consistent with the various diagnoses were administered, such as peripheral vasodilators, Buerger's exercises, supports for the transverse arch, and physiotherapy. These all proved of little avail.

Finally consideration was given to the possible desirability of arthrodesing the proximal interphalangeal joints of the three outer toes, or of amputating these, the only alternative being a stoical acceptance by the patient of his disability. The patient, having a stable personality, decided to exercise fortitude.

THE PROBLEM IS SOLVED

I did not see him again for almost two years, and then he had an interesting story. He said he now had difficulty in writing and shaving with his right hand, that his right leg moved with less facility than his left, and that when walking he would find his right arm motionless by his side; even when he made it swing it soon ceased to do so when his attention was diverted.

The diagnosis was now easy—hemi-Parkinsonism. Of course, I then made haste to read Walshe's account of Parkinson's disease in his 'Diseases of the Nervous System,' and was thrilled to find that in this disease the patient may complain of 'painful flexion cramps in the toes'. The diagnostic picture was complete. My patient was seen soon afterwards by a neurologist, who confirmed the diagnosis of hemi-Parkinsonism which, he considered, was probably of cerebrovascular origin although, as he said, 'the peripheral vessels were not very much thickened and his blood pressure was only 140/90'. Anti-Parkinson drugs were immediately prescribed, and during the sixteen months which have since elapsed there has been only a slight increase in muscle rigidity; the impaired mobility of the right side of his

face is now more obvious, and tremor remains negligible. The right foot is probably less painful on walking short distances, but active movements of the toes will quickly provoke painful flexion cramps, even if the patient is otherwise at rest.

FUNCTIONAL FOOT DISABILITIES

By W. SIMPSON, M.B., Ch.B.
*London, N.*14

We all have 'bees in our bonnets'—at least that is what our friends call them. Mine is that the medical profession does not understand the mechanism of the human foot. A surgeon, in the dim and distant past, made the statement that the disabilities of the foot that plague mankind were due to ill-fitting shoes. Taking the statement on its merits, it is odd that the whole of mankind should wear ill-fitting shoes. As I have seen these identical deformities in the feet of Negroes and Chinese, who have never worn shoes, the whole idea is exploded.

THE CAUSE OF THE TROUBLE

I am now convinced that the whole cause of the trouble is as follows. We all have the anatomy of a four-footed mammal and we have to adapt that anatomy to a two-footed existence. When a child begins to walk, he always keeps his feet well apart with the knees bent, as he knows instinctively that this is the only way that he can fully use the great toes. A chimpanzee walks similarly. When the feet are brought close together in walking or standing, we come off those strong useful toes and never fully use them again. The weight of the body is now transferred to the heads of the metatarsal bones of the 2nd, 3rd, and 4th toes. This part of the foot is incapable of bearing the weight of the body and collapses sooner or later, thus initiating hammer-toes, as the corresponding toes are drawn up. If the collapse extends far enough, the feet go flat.

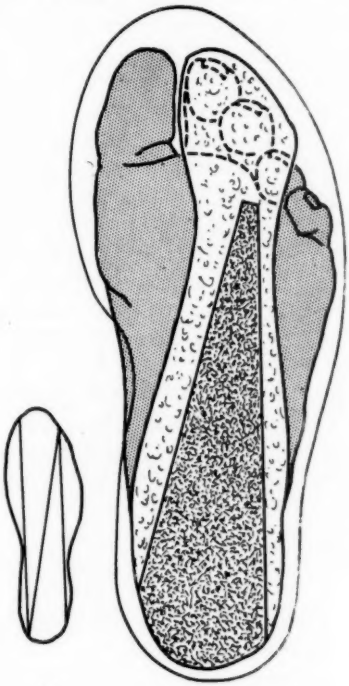
The great toes, now virtually unemployed, 'squint' in a similar manner to a squinting eye (the eye squints because it is not used on account of a lens defect). The great toe now pushes against the rest of the toes and interferes with their movements. The 5th toe is then compressed against the outer side of the shoe and, sooner or later, a corn results. If the angle of the great toe becomes acute enough, the pressure of the joint proximal to it on the inner side of the shoe (the metatarso-phalangeal joint) will produce a bunion by pressure on the shoe. The collapsed metatarsal heads, by pressure on the underlying skin of the sole of the foot, will eventually cause thickening which is at first protective, but, sooner or later, will cause pain in the sole. An ingrowing toe-nail is caused by the pressure of the great toe on the second toe, depending upon the angle.

In order to prevent or treat corns, callosities, bunions, ingrowing toe-

nails, and flat feet, all that is required is to allow the individual to use the great toe to the full.

THE REMEDY

I have devised a modified insole which does this perfectly (fig. 1). I use an ordinary cork insole, which can be purchased for 8*d*. a pair. I take a large one (size 10 or 11) and, with a ruler, draw two parallel lines and join



(a) (b)

FIG. 1.—Diagram of modified insole.

the ends with a straight diagonal line. I then cut two thin triangles, by following the lines with scissors. The triangles are shaped as shown in the diagram (fig. 1a). The principle is to keep pressure off the great toe and the 5th toe, and the blunt apex of the triangle raises the 4th metatarsal head, puts a slight tilt on the foot and allows the metatarsal joint of the great toe to come down and function fully.

The modified triangles are fixed to the under surface of the insoles with a suitable adhesive (I use shoemaker's paste) in the position shown in the diagram (fig. 1b). The insoles are cut with a long curve on the inner side and a shorter one on the outer, to prevent interference with the 1st and 5th toes.

MEDICAL JARGON

THE OSLERIAN ORATION 1958

By SIR ERNEST GOWERS, G.C.B., G.B.E., D.Litt.

I HOPE that my choice of subject will not be taken to imply any slight on the medical profession. On the contrary, as I address myself to the task entrusted to me, the two members of that profession who must be uppermost in my thoughts were both masters of luminous prose—the great man whose memory your Society exists to honour, and my own father. Both wrote textbooks that are still read, not only for their matter but also for their manner. I think it must have been works such as theirs that Sir Francis Walshe was thinking of when in a recent address he advised his listeners to read some of the medical books and papers published between 1870 and 1920, saying that

> 'their lucidity and coherence are not simply a gift from the Gods, but the fruit of sweat and toil, of constant rewriting and pruning, until every sentence contained a maximum of clarity in a minimum of words'.

My father was always a stickler for plain words; his bluntness in using them and his intolerance of woolly thinking were sometimes a source of embarrassment to his family, and, I suspect, occasionally of discomfiture to his housemen and even his patients. One of these, an old Methodist minister, told me years ago about an experience of that sort. My father asked him whether he had a pain somewhere or other. The old gentleman, whose calling had no doubt bred in him scrupulous care in telling the exact truth, reflected a short while and then replied: 'No, Sir William, not exactly a pain but a sensation equivalent to pain'. He told me that the sharpness of my father's reaction to that well-meant reply was positively alarming.

DEFINITION

If I am to talk about jargon I ought to begin by explaining what I mean by the word; it is always as well to define one's terms, especially when they have as roving a disposition as this one has.

I shall confine jargon, at any rate to begin with, to its well-recognized meaning of technical terms peculiar to particular pursuits—arts, sciences, professions, trades, games or any other branch of human activity—an esoteric vocabulary not ordinarily understood by outsiders. I deprecate the present tendency to broaden the meaning of the word beyond all reason by using it as a term of abuse for any style of writing that one thinks inferior to one's own. It is bad for a language when the sharp edges of its words are blunted. I know that jargon originally meant a confused and unintelligible noise applied particularly to the chirping of birds—their 'sweet jargoning' as the Ancient Mariner called it. Perhaps that is the justification that doctors would plead to a charge of contributing to the blunting process by coining

the expression *jargon aphasia* for the utterances of patients suffering from a condition that makes them talk rather like the narrator in 'Finnegan's Wake'. But their sort of talk would be more suitably called gibberish, and I do not suppose it could often be described as *sweet*.

That energetic crusader for plain speech, Ivor Brown, once propounded the theory that jargon is a sort of uniform. He said:

> 'The English love to wear ritual clothing and so cherish a ritual verbiage too. The barrister will not put away his wig: the parson has his dog-collar, the official has his pin-stripe trousers. There is a gobbledegook of the Law, of Theology, of Finance, of Sport, of Criticism. The users will no more drop the lingo than they will abandon the insignia and haberdashery of their professions'.

A PROTECTIVE MECHANISM

Perhaps the reason why he does not include doctors is that they are an exception to the rule of sartorial conservatism. They have abandoned the top hat and frock-coat that used to be the insignia and haberdashery of their profession. But there is little sign that this has been accompanied by an equal readiness to discard their ritual verbiage. There are, indeed, some among you who say that the more you have shed the one the more you have come to rely on the other as a sort of protective mechanism. The doctor who writes so agreeably in *The Spectator* every week has gone so far as to assert that much medical writing is pompous, repetitive and makes use of polysyllables when a plain word would do. He conceded that long rumbling words with a Latin or Greek root sound more learned, but did not hold that to be a good reason for preferring them. Nor would he allow any usefulness nowadays to medical jargon for the purpose of mystifying the patient. The patient, he said, is more fly than he used to be. I suppose that is true, but it is also true that, so long as doctors continue to write their prescriptions in cabbalistic symbols unintelligible to us, we are unlikely to shake off all trace of that feeling towards them which the magic of the primitive medicine-man must have inspired in his patients.

I myself speak with natural diffidence on such a subject, but my own very limited observation does suggest that there may be something in what *The Spectator* doctor says. In the now distant days when I was young there were children's doctors but no pædiatricians, ear-nose-and-throat surgeons but no otorhinolaryngologists, skin doctors but no dermatologists, mad doctors but no psychiatrists. I am not questioning the propriety of this metamorphosis of those who follow these specialties if they think it helps them in carrying on their beneficent work. The mad doctor in particular may reasonably have wanted to get rid of so crude and ambiguous a designation. Indeed it is not thought nice any longer to use the word *mad*. *Mad* and *lunatic* are held to imply an outmoded approach to psychological problems: and so our lunatic asylums have become mental hospitals and our criminal lunatics Broadmoor patients, just as what used to be backward and troublesome boys and girls have become maladjusted adolescents.

That, I am sure, is all very right and proper, though I think our love of

giving tainted things new names in the hope of removing the taint may incline us to attribute to words a greater power than they have any business to possess. But the habit of rejecting old and simple words in favour of new and learned ones does tend to increase the difficulty of communicating thought from one mind to another, and can be overdone.

A FREAK EXAMPLE

Some years ago a doctor friend pointed out to me a remarkable example of medical jargon pilloried in *The Lancet*. I was so much impressed by it that I put it into a book ('The Complete Plain Words', p. 54). I quote first *The Lancet's* translation of the passage into simple English. It runs:—

'Experiments are described which demonstrate that a normal person can taste sugar in water in quantities not strong enough to interfere with his sense of smell or take away his appetite'.

Why this fact should have been thought worth demonstrating by experiment I cannot say. Perhaps it was a consciousness that the experiment was not of outstanding importance that led the writer of the treatise to dress up the result as he did. What he wrote was:—

'Experiments are described which demonstrate that in normal individuals the lowest concentration in which sucrose can be detected by means of gustation differs from the lowest concentration in which sucrose (in the amount employed) has to be ingested in order to produce a demonstrable decrease in olfactory acuity and a noteworthy conversion of sensations interpreted as a desire for food into sensations interpreted as a satiety associated with ingestion of food'.

That is of course a freak example, and it is only fair that I should tell you it comes from America. But have we not some cause to search our consciences here too?

SOME PERTINENT QUERIES

This question occurred to me when I recently had occasion to make a superficial study of what progress had been made in the last fifty years or so in our knowledge of the cause and cure of a certain disease that is still found baffling. I read what both modern textbooks and old ones had to say about it. I noticed a certain difference in verbal style. Let me give you one small example. In a lecture delivered in 1886 this advice is given. 'The patient can walk with assistance and should be encouraged to do so'. I found in an article written in 1951 the same advice but in different words: 'There is no need for bed all the time; the patient should be advised to take intermittent ambulation'. Have such changes in terminology any symptomatic significance? I know, of course, that it is foolish to protest against the use of the word *ambulant*. I shall be told with justice that the phrase *early ambulation* expresses a therapeutic principle more conveniently than it could be expressed in any other way. But are not these 'long rumbling words with a Latin or Greek root' apt to take the reason prisoner? The friend I mentioned just now once sent me a copy of an address to his students on 'The Seven Sins of Medicine', and I was interested to find that he gave them this advice about the sin of obscurity:—

'When a patient says to you, "If I go half-way up a hill I feel I'm done for", record it in your case history in those words, do not say, "The patient complains that during ambulation up a moderate incline, he suffers a feeling of impending dissolution" '.

And when at another time I read of a certain patient that so long as he remained in bed he showed no improvement but from the day of ambulation onwards he did, I wondered whether the simple phrase 'when he got up' might not have conveyed the writer's meaning equally well. Perhaps even better; 'the day of ambulation' has an oddly theological ring, vaguely suggesting the day of resurrection.

Let me pose one or two other queries from my own random reading even at the risk that they will serve merely to expose my ignorance of medical matters. When you describe the result of a drug on a patient, is it really clearer to say that it had a facilitating influence than that it helped? When a patient is asked the meaning of certain words to test his intelligence is it important to describe those words as of medium rating on basic intelligibility rather than as fairly simple ones? Is it more precise to say that certain unexpected symptoms did not effect disconfirmation of your diagnosis than to say they did not show it was wrong? Is a statement that a certain condition is caused by excessive food intake really different from saying that it is the result of overeating? And is it necessary to use that ugly neologism *contra-indicated*, which seems to be becoming such a favourite with men of science? I find it hard to believe that to say that such-and-such a treatment is contraindicated is anything more than a ritualistic way of saying that it is unlikely to do any good.

I do not know whether the young woman who is going to have her first baby would be pleased or offended to know that in your eyes she is a primigravida; perhaps she would be pleased; it suggests, like prima donna and prima ballerina, some notable accomplishment. But I am pretty sure that her less fortunate sister would resent being called nulliparous, and one who had gone to the other extreme would think that the label multiparous indicated a rather inhuman approach to her experiences. Nor again can I pretend to be sure whether a description of a patient as suffering from intermittent claudication is different from saying he goes lame from time to time. On the other hand, it is certainly refreshing to come across a reference to what I gather is called the burning feet syndrome in cases of liver disease, and to think how stoutly whoever first observed that symptom must have fought against the temptation to coin some such word as *phlogeropodic* for it.

THE REAL MISCHIEF

But I recognize that it is presumptuous for an outsider to pass judgment on jargon so long as it is kept in its proper place. There it is often indispensable, though even an outsider may be permitted to wish that there were more men of science of the same mind as Julian Huxley, who has said that when he wants a term for a new concept he prefers if possible to take over a

familiar word rather than to coin a new piece of esoteric jargon. The real mischief is that jargon does not keep in its place; it is constantly escaping. Occasionally, it is true, it does so usefully, as the words *diagnosis* and *stymie* have escaped from medicine and golf to become valued members of the general vocabulary. But more often these migratory words are misunderstood, misapplied, done to death and corrupt common speech. The medical terms *hectic* and *chronic* are familiar examples of words that have been thus vulgarized. Why jargon exercises so strong a fascination over the popular mind I cannot say; this might be an interesting study for psychologists. Perhaps it appeals to that desire to show off which, according to a famous contemporary philosopher, is one of the strongest natural impulses of all male human beings. Moreover, we live in a scientific age and we like to give the appearance of thinking and speaking in a scientific way. New sciences proliferate, especially within that wide field embraced by the term sociology. No doubt this ambition is laudable, but it can be carried too far. Questions we were once simple enough to think needed no more than common sense for their solution are now approached by the scientific method; and this sometimes seems to consist of laboriously collecting a mass of information in order to prove statistically the truth of something every sensible person already knows must be true and whose truth or falsehood does not matter much anyway.

THE VERBAL SINS OF THE NEW SCIENCES

It is the new sciences more than the older that are corrupting our language. They must have new words for their new concepts—or it may sometimes be, one suspects, to give a new look to an old one. I feel sure, for instance, that there must be some old and simple word for what I find described in a well-known sociological book as 'bilateral erotic experiments outside marriage'; the idea is not new. The boundaries of these sciences are ill-defined and jargon easily escapes over them. Thus it spreads into general speech, creating what Fowler used to call *popularized technicalities* —vogue words whose meretricious attraction drives out others that have served us long and faithfully. We can no longer have bees in our bonnets; they must be complexes. If we are in that embarrassing state of mind we used to call having mixed feelings we must not use that expression; we must say we are suffering from ambivalence. No-one is shy any more though he may be inhibited. We are no longer affected by our circumstances though we may be by our environmental factors. We do not take an instinctive dislike to things and people though we may find ourselves allergic to them. We ask a friend for his reaction to an idea of ours, not what he thinks about it. We are old-fashioned if we say of some project that it is likely to succeed; we must now say that it is viable. Creeds have become ideologies and heretics deviationists. We do not commit sin any more; it looks as if we should have to revise the Lord's Prayer and make it run 'Forgive us our unethical behaviour as we forgive them that behave unethically to us'. What were once

hardened sinners are now recidivists; we do not try to reform them but there is a chance that they may be rehabilitated. We must not speak of the poor, though we may of the lower income brackets or the underprivileged classes. What that last ridiculous expression means is presumably known to whatever sentimental politician invented it but by the rest of us can only be guessed.

A MIASMA OF VERBAL ABSTRACTIONS

I have in my collection of curiosities an exceptionally choice specimen of the miasma of verbal abstractions that is apt to envelop what Ivor Brown has called those 'Uplifters and Welfarists who dabble vaguely in social sciences'. It is about the bringing up of children. It is an account of a serious study and I am sure I should find it interesting if I could discover any meaning in it. It begins at the very beginning and explains the mystery of conception. The fertilization of the ovum is, it says, the result of the 'exclusive electivity of dynamic specificity'. That process having been made perfectly plain, we come to the child itself and its nature is unfolded. It is 'the supreme and most concrete example of an origination or novelty from the fusion of two diversities'. It is 'a new and unique individuality that is originated through the bipolarity of organismal function'. Turning to the position of the child in the family, we are reminded that 'a functional unity can be maintained in the face of a dispartite organism' and that the development of the child within the family proceeds through 'mutual synthesis carried on through a functional zone of mutuality'. But we are warned that 'reserves that are occupied in a continuous unidirectional adjustment of a disorder are no longer available for use in the ever-varying interplay of organism and environment in the spontaneity of mutual synthesis'. And so on to the end of the story.

This must be the sort of thing that Lionel Trilling was thinking of when he wrote:

> 'A spectre haunts our culture. It is that people will eventually be unable to say "We fell in love and married", let alone understand the language of *Romeo and Juliet*, but will, as a matter of course, say, "Our libidinal impulses being reciprocal, we integrated our individual erotic drives and brought them within the same frame of reference" '.

Another eminent man of letters, brooding over this phenomenon, has said that he sometimes wonders whether civilization will not come to an end because no-one will understand what anyone else is saying. That failure in communication will not be made any better by a lurking doubt whether the person saying it knows himself. It is as though we were building a new Tower of Babel. But there will be this difference. The confusion of tongues that we read about in the Book of Genesis was imposed as a penalty for breaking the building regulations in force at the time—a curiously inappropriate punishment, one would have thought, and not one that the culprits could have reasonably been expected to foresee. But this time we shall have wantonly brought it on ourselves.

A WIDELY PREVALENT DISEASE

In conclusion I should like to narrow my view by going back to the medical profession and to enlarge my subject by speaking of jargon in its more popular sense of a style that, for whatever reason, fails to make the writer's meaning clear. I expect I have said some things that some of you do not agree with. But there is one thing none will question. That is that jargon in this sense is a disease widely prevalent today, that the young are specially susceptible to it, and that it is the duty of those who educate future members of your profession to provide them with every possible prophylaxis; for there is, I suppose, no calling in which clarity of thought and exactness of communication are more vitally important.

Fifty years or so ago, when Sir William Osler was Regius Professor at Oxford, his opposite number at Cambridge was a hardly less remarkable man, Sir Clifford Allbutt. Like Osler, he did not confine his interests to his profession. He was a classical scholar and a man of wide culture. The experience of reading innumerable theses by medical students moved him to publish a little book that he called 'Notes on the Composition of Scientific Papers'. Its purpose was to enforce the lesson, as he says in his preface, that, 'though composition is painful, the man of science ought best to know that style and matter can no more be dissociated than skin and bone; that if we write clumsily, loosely or disjointedly our thoughts also are undisciplined; for the sifting of language is the weighing of thought and in scientific prose words should be used as carefully as symbols in mathematics'. (My father once struck the same note when, in opening a session of University College Hospital Medical School, he told the students that they would do well to add a course in formal Logic to their medical studies.) 'Yet', Allbutt goes on, 'I note that many of my candidates are content with one general noun, ***question***, two adjectives, ***marked*** and *localised*, two verbs, *occur* and *involve*, one adverb, ***markedly*** and one conjunction, ***while***—words so worn that they become mere counters'. At the same time the jargon disease must even then have been showing itself, for he observes that the tiro conceives that to express himself effectively he must fetch words from afar and weave them into a highly complex web. Speaking of what was then I suppose an infant science, learning to walk with uncertain steps, he says 'The psychologists are sad dogs in this kind of vagueness and equivocation'.

In some respects changes in usage have made the book out of date. But everything that matters is still there—all those principles that Fowler and others have since preached as the essentials of clear, accurate and vigorous writing. If the General Medical Council were to have the book revised and reprinted and prescribed as a compulsory subject in one of the M.B. examinations, the doctors of the future might learn at the outset of their career the truth put thus by Allbutt in the words with which he ends:

'Force, lucidity, unity, simplicity, economy of expression are virtues which we may all attain; originality will be as God pleases'.

CURRENT THERAPEUTICS

CXXIX.—SULPHAMETHOXYPYRIDAZINE

By GEORGE GEE JACKSON, M.D.

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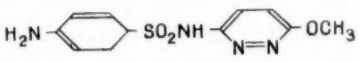
SULPHAMETHOXYPYRIDAZINE ('lederkyn', 'midicel') is a new antimicrobial sulphonamide with certain pharmacological properties that offer potential advantages over other sulphonamides. It is these properties and not any significant difference in its antimicrobial spectrum or activity from the pyrimidine-containing sulphonamides that makes sulphamethoxypyridazine noteworthy. Significant alteration of pharmacological properties without diminishing antibacterial activity in comparison with sulphadiazine represents a major development in chemotherapy. The properties of sulphamethoxypyridazine that are of special importance are: absorption from the gastro-intestinal tract, poor acetylation in the body, diffusion into extracellular fluids, very low renal clearance, relatively high solubility among sulphonamides in acid urine, and antibacterial activity equal to sulphadiazine.

The medical indications for sulphonamide therapy have evolved from the clinical experience of the past 23 years since announcement was first made of the experimental and clinical value of 'prontosil'. The introduction of a new sulphonamide with the properties of sulphamethoxypyridazine does not allow a major change in these indications. It does permit the anticipation of effective—perhaps more effective—treatment as a result of continuous plasma concentrations of free sulphonamide after a single daily or, in some cases, a weekly dose and of less difficulty from crystallization of the drug in the urine, which has been a significant complication of treatment with many sulphonamides. Another beneficial effect of the new compound has been to renew the interest of scientists and clinicians in a critical evaluation of the role of sulphonamides among present-day therapeutic agents.

CHEMISTRY

Sulphamethoxypyridazine is a generic name for the compound, 3-sulphanilamido-6-methoxypyridazine, which has the following structural formula:



It is a light yellow powder which is soluble in neutral aqueous solution. At pH 5 or 6 it is approximately ten times as soluble in water as sulphadiazine: i.e. to the extent of 100 to 150 mg. per cent. The acetylated derivative, 3(N^4-acetyl)-sulphanilamido-6-methoxypyridazine, is only about one-third as soluble in aqueous solution as the parent sulphonamide, but acetyla-

tion *in vivo* occurs slowly and the conjugated form is preferentially excreted in the urine.

PHARMACOLOGY

Absorption of the drug from the gastro-intestinal tract, as judged by recovery in the urine, compared with recovery after intravenous administration, seems to be complete. Usually more than 70 per cent. of the total drug administered can be accounted for in the urine. It is excreted as free sulphonamide, acetyl or glucuronide conjugated forms, and in the form of several aryl amine derivatives.

The peak plasma concentration of sulphonamide in humans is usually attained four to six hours after a single dose. At this time the drug level is quite uniform over a fairly broad range of dosage. The time, height and duration of the maximum concentration are related to the size of the dose. Approximately 10 per cent. of the drug in plasma is in the conjugated form. About 50 (plus or minus 10 to 15 per cent.) is bound to the plasma proteins. The proportion of protein-bound drug is inversely related to the drug concentration. Unbound sulphamethoxypyridazine diffuses freely into extravascular fluid including the cerebrospinal fluid, in which it attains a concentration of 10 to 20 per cent. of the total plasma level (Boger *et al.*, 1956). On the other hand, there is little or no penetration of the drug into erythrocytes (Nichols *et al.*, 1956).

Excretion and renal clearance.—Sulphamethoxypyridazine is excreted slowly but almost entirely by the kidneys. The rate of excretion is related to the plasma concentration and not to the rate of urine flow. Water diuresis, or the concentration of acids in the urine is without influence. The excretion rate is affected only slightly and variably by alkali administration or by giving carbonic anhydrase inhibitor (Nichols and Finland, 1957). The ratio of free to conjugated drug excreted is an individual variable. Some patients excrete as much as 90 per cent. of the total urine content as free sulphamethoxypyridazine, but usually only one-third to one-half of the total is unchanged.

The renal plasma clearance for free sulphamethoxypyridazine is only 2 to 3 ml. per minute and is influenced little by the plasma concentration of drug (Jackson and Grieble, 1957). Individuals vary in this function over a relatively narrow observed range of 1 to 6 ml. per minute. The same person may vary the renal clearance of a second or subsequent dose. The mechanism of excretion is assumed to be glomerular filtration but it is evident that avid reabsorption of sulphamethoxypyridazine occurs in the renal tubule and 95 per cent. or more of the filtered load of free sulphonamide is reabsorbed. In these circumstances it is difficult to recognize whether there also is tubular secretion and, although there is no evidence for it, the possibility cannot be excluded. The conjugated form of sulphamethoxypyridazine is cleared by the kidney at four to ten times the rate of free drug, or 10 to 20 ml. per minute for most people. This differential excretion maintains a low plasma level of conjugated drug and accounts for the relatively high

proportion of conjugated sulphonamide in the urine. Because the renal reabsorption of sulphamethoxypyridazine is nearly complete, persons with mild or moderate renal insufficiency accumulate only slightly higher concentrations in the blood, about 10 per cent. greater, than normals, and this is largely retention of the conjugated form.

DOSAGE

From previous experience and from experimental data it has been assumed that the optimum dose of sulphamethoxypyridazine should yield a plasma

Authors	Dosage regimen	Average plasma concentrations of free SMP		
		Days of treatment	Sample	mg.%
	Children			
Lepper *et al.* (1957)	30 mg./kg./week	random	trough	1.83
Weihl (1958)	15-20 mg./kg./day	random	random	6.4*
Ross *et al.* (1957)	50 mg./kg./day	5	peak	16.0*
			trough	8.0*
	Adults			
Finland *et al.* (1957)	1.0 g. daily	15 to 21	peak	6.4*
			trough	2.4*
Nichols and Finland (1957)	1.0 g. daily	random	peak	12.5
			trough	5.0
Jones and Finland (1957)	0.5 g. 12-hourly	7 to 8	peak	6.3*
			trough	6.0*
Walker and Hamburger (1957)	0.5 g. 12-hourly	random	trough	5.2*
Walker and Hamburger (1957)	1.0 g. four times daily	random	trough	6.2*
Finland *et al.* (1957)	1.0 g. four times daily	7	peak	8.7*
			trough	6.0*
Walker and Hamburger (1957)	1.0 g. 12-hourly	random	trough	12.0*
Frisk and Wassen (1957)	1.0 g. 12-hourly	7	—	15.4*
		2	—	5.4*
Finland *et al.* (1957)	1.0 g., then 0.5 g. four times daily	7	peak	6.0*
			trough	4.5*
Prlina *et al.* (1958)	1.5 g., then 0.5 g. four times daily	2 to 4	—	10.0
		5 to 15	—	6.0
Finland *et al.* (1957)	2.0 g., then 1.0 g. four times daily	10	peak	9.7*
			trough	6.7*
Prlina *et al.* (1958)	2.0 g., then 1.0 g. four times daily	2 to 15	—	6 to 20
Grieble and Jackson (1958)	2.5 g., then 0.5 g. four times daily	7 to 250	random	10.1

*Concentration in whole blood given; plasma concentration is approximately one and a half times as high in the absence of anæmia.

TABLE I.—Some reported observations on the plasma concentration of sulphamethoxypyridazine following oral administration of multiple doses.

concentration of about 10 mg. per cent. free sulphonamide. Some reported observations on the concentration of sulphamethoxypyridazine in plasma or whole blood of humans given multiple doses under a variety of regimens are given in table I. On the basis of these data a single daily dose of 25 mg./kg. should maintain the desired plasma concentration in most

infants and children. It should be emphasized, however, that all the studies have shown significant variation among individual patients. In adults a single daily dose of 0.5 or 1.0 g. is adequate to maintain an effective level. A larger initial dose or more frequent doses during the first few days of therapy seems desirable.

THERAPEUTIC EFFECTIVENESS

The treatment of experimental infections in laboratory animals has verified the potent *in vitro* antibacterial effect of sulphamethoxypyridazine. Bacterial infections induced with strains of pneumococcus, streptococcus, Pasteurella or Klebsiella responded well to oral dosage (Roepke *et al.*, 1957). Comparison with the results obtained with sulphadiazine indicated that the drugs were equally effective on the basis of blood concentrations.

The widest clinical experience with sulphamethoxypyridazine has been in the treatment of acute and chronic infections of the urinary tract (Grieble and Jackson, 1958; Frisk and Wassen, 1957; Walker and Hamburger, 1957; Prlina *et al.*, 1958; Ross *et al.*, 1957). The drug has also been used in the treatment of respiratory infections, including lung abscess, dysentery, meningitis, cellulitis, and trachoma (Ross *et al.*, 1957; Walker and Hamburger, 1957; Daeschner *et al.*, 1957; Terrell *et al.*, 1957; Bietti, 1957; Weihl, 1958). Patients with rheumatic fever given sulphamethoxypyridazine for prophylaxis against streptococcal infections remained free of such infections (Lepper *et al.*, 1957). In all these instances the clinical results were at least equivalent to those expected with sulphadiazine. Meningococci are uniformly inhibited; pneumococci, hæmolytic streptococci and gonococci are usually inhibited. Fifty to 70 per cent. of strains of *E. coli* are sensitive to sulphamethoxypyridazine and such infections quickly respond clinically. As with other sulphonamides, infections with *Aerobacter aerogenes*, proteus, and pseudomonas have responded poorly, if at all, and staphylococcal and enterococcal infections are seldom cured by sulphamethoxypyridazine.

TOXICITY

Adverse reactions which commonly occurred with earlier sulphonamides also occur with sulphamethoxypyridazine, except that nephrotoxicity from crystalluria has not been a problem. The most significant reactions are a skin rash and drug-induced fever. Headache has been the most common complaint, but this has rarely required discontinuation of treatment. Stomachache, vomiting and dizziness are symptoms that have been temporarily related to sulphamethoxypyridazine in some patients. Untoward reactions can be expected in about 6 per cent. of patients. The amount of drug given and the plasma concentration have some relationship to the incidence. Most of the reactions occur after several days of therapy and usually before three weeks. Chronic toxicity has not been a problem.

The skin rash is erythematous, maculopapular, sometimes pruritic, and likely to involve both the trunk and extremities. Fever of around 101°F. (38.3°C.) or higher may occur after several days in the initial course of

therapy or quickly upon retreatment. Hypersensitivity of the anaphylactoid type is possible on readministration of the drug to a sensitized person. There appears to be little or no cross-sensitivity with sulphadiazine or sulphafurazole. Manifestations of drug toxicity disappear quite rapidly when administration of the drug is discontinued. No significant blood dyscrasias, exfoliative dermatitis, neurological or renal toxicity have been reported.

COMMENT AND SUMMARY

Chemotherapy with the sulphonamides has remained as the treatment of choice for certain infections throughout the era of predominance of antibiotics. Among bacterial infections, meningococci, some bacillary dysentery, and colon bacillus infections of the genito-urinary tract can be classified in this group. Among viral diseases, trachoma, and among fungi, nocardial infections might also be treated preferentially with a sulphonamide. In all of these conditions, and others of more elective choice, the properties of this new sulphonamide should be an asset. Outstanding among these properties are the slow rate of excretion and poor acetylation, which permit the use of a single daily dose to maintain a constant antibacterial concentration of free sulphonamide in the plasma. The ease of administration makes long-term treatment readily acceptable. Further, in common with other sulphonamides, sulphamethoxypyridazine diffuses readily with extracellular body water and is excreted almost entirely by the kidneys. Its relatively greater solubility in acid urine appears to be sufficient to eliminate the dreaded complication of concretions or renal toxicity from crystalluria.

This new agent does not overcome some drawbacks of sulphonamides. This group of drugs is primarily bacteriostatic, and many strains of bacteria or other micro-organisms are resistant to their inhibitory influence. Skin rash, fever, and hypersensitivity reactions must be expected in some patients. The new agent is an improved tool. It is a potentially double-edged instrument, and will contribute most by limited precise use.

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MINOR SURGICAL PROCEDURES

IX.—INGROWING TOENAIL

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Although it is an apparently trivial disorder, an ingrowing toenail may yet be responsible for weeks or even months of painful disability. A better understanding of the anatomy of the nail and the abnormalities of its growth may help to relieve pain and to prevent ingrowth of the nail and its septic complications.

ANATOMY AND PATHOLOGY

The normal nail develops from a germinal matrix which lies at the root of the nail deep to the lunula and deep to the nail fold. It extends laterally to the nail grooves (fig. 1A) and a little beyond them. Normally, the free edge of the nail projects clear of the nail grooves.

The ingrown toenail is often less curved in its transverse plane than usual. At its free edge the nail is found deeply embedded in the nail groove on one or both sides. Commonly, a sharp spicule of nail projects from the corner of the nail and grows deeply into the sensitive nail groove (fig. 1B). Occasionally, the nail appears sharply incurved along the whole length of the lateral edge of the nail.

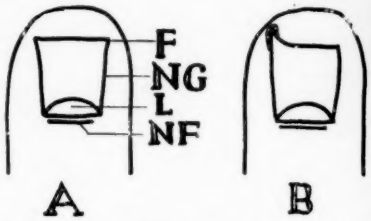


Fig. 1.—A. Nomenclature of the nail: F, free edge; NG, nail groove; L, lunula; NF, nail fold. B. Diagram of an ingrowing toenail.

Initially the nail groove is uninfected but, following the continuous irritation of the sharp edge of the nail, it becomes acutely inflamed and eventually suppurates. An exuberant growth of granulation tissue may appear along the side of the nail and this makes any minor treatment of the nail difficult or ineffective. With continued suppuration, the nail becomes loosened by the pus beneath it and a typical paronychia may result.

ETIOLOGY

Ingrowing toenails may cause trouble at almost any age but most commonly in the second and third decades. Men suffer from the condition as often as women. The great toes are most liable to be affected (fig. 2) but it is not uncommon to find the second toes also involved. One or both edges of the nail may grow into the nail groove but there is a tendency for the outer

side to grow in more often than the inner. Usually, both great toenails are affected although complaint may be made of only one.

The wearing of ill-fitting shoes or boots is usually cited as the cause of abnormal growth of the nail. Tight shoes may crowd the soft tissues of the toe over the edge of the nail and permit its penetration into the skin. Such a history, however, is rarely obtained and it is more likely that, as the toe is pressed down during walking the soft tissues alongside the nail ride up around the nail. High-heeled shoes may exaggerate this effect. In addition, if the corner of the nail is left sharp after being cut, it may become embedded in the nail groove. Probably the most important factor is cutting the nail too short and leaving sharp corners at the free edge of the nail.

FIG. 2.—Photograph of an ingrowing toenail. There are prominent granulations along the inner nail groove; the outer groove is swollen with inflammation.

A congenital abnormality of nail growth is unlikely to be solely responsible as the condition is rarely to be seen in young children. On the other hand a family history of ingrowing toenails is sufficiently common to suggest the possibility of an inborn predisposition.

A severe crushing injury of the toe may be followed some months or years later by an ingrowth of the nail but usually this occurs in association with onychogryphosis. The thickened nail tends to be more arched transversely than usual and its edges may grow into the nail grooves.

CONSERVATIVE TREATMENT

Prophylaxis.—Prophylaxis is best achieved by proper cutting of the nails so that the terminal edge of the nail is cut transversely to its corners and no sharp spicules are left to grow into the nail grooves. The nail must not be cut too short but must be allowed to project free of the nail grooves.

Uninfected ingrowing toenail.—Before infection arises, the ingrown toenail causes pain during movement as the edge of the nail digs in to the sensitive nail groove. It is most important that effective treatment should be carried out during this phase as it is then possible to prevent development of infection. Numerous measures have been advised. Ingenious manœuvres, such as paring down the centre of the free border of the nail, or cutting a V-wedge out of it, have been recommended to decrease pressure on the lateral edges of the nail. Laying a strip of thin metal foil deep to the edge of the nail, in the nail groove, seems a simple remedy to protect the skin

beneath the edge of the nail, but it is difficult to keep in place.

The cause of pain is the sharp spicule of nail which projects from its edge. The easiest way of dealing with this is the obvious one of cutting it away. With a sharp pair of pointed scissors it is possible to lift the nail

FIG. 3.—Method of removing the corner of an ingrowing toenail.

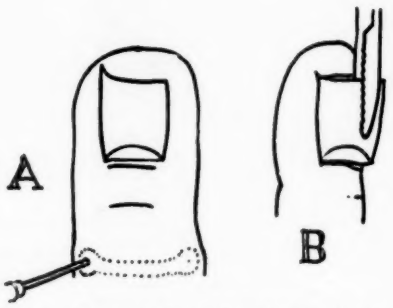


FIG. 4.—Removal of a nail under local anæsthesia. A, ring block; B, avulsion of nail.

edge free of its groove and, by cutting proximally and obliquely, the offending sliver of nail may be removed (fig. 3). It is then essential to see the patient regularly and to cut the edge of the nail obliquely until the free border of the nail projects clear of the nail groove. The value of this method is that pain is relieved immediately and, if it is followed up conscientiously, a cure may be achieved. Ideally, this treatment should be given by a chiropodist, but this may be expensive for the patient as hospitals are often unable to provide a chiropody service and treatment can only be obtained privately. It is obviously impossible for the patient to cut the nail for himself and so it is probably best that his doctor should see him regularly and prevent the nail from growing in.

Infected ingrowing toenail.—A minor degree of infection, with moderate erythema or œdema, may be relieved by cutting the nail in the way that has been described. Once pus is present, however, there is only one satisfactory means of treatment and that is the removal of the nail. It is useless to administer antibiotics as the sharp edge of the nail will aggravate the inflammation so long as it is present.

The nail can be removed under local anæsthesia by the use of a ring block. Local anæsthesia is perfectly safe so long as inflammation does not extend beyond the distal interphalangeal joint. After sterilization of the skin, lignocaine (2 per cent.) is injected into the subcutaneous tissues at the base of the toe. Injections are made into the dorsum of the toe at two sites, one on either side of the midline (fig. 4A). Enough local anæsthetic is injected to distend the subcutaneous tissues firmly. Several minutes must elapse before complete anæsthesia is achieved, much longer than is

necessary for a similar block of the finger. To remove the nail, all that is necessary is to insert one blade of a pair of artery forceps beneath the nail, on the side of infection. The forceps is then closed and rotated so as to avulse the nail (fig. 4B). The nail bed is cleaned with cetrimide, and a non-

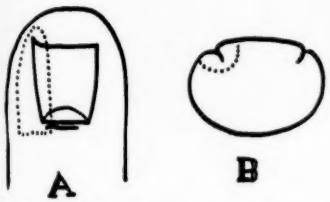


FIG. 5.—Wedge excision of the nail and its bed.

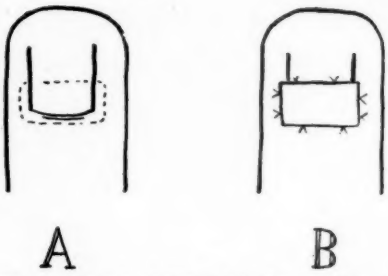


FIG. 6.—Repair of defect left after excision of nail bed. A, excision of the nail bed; B, repair by a skin graft.

adherent paraffin gauze dressing is applied. The nail bed becomes insensitive remarkably quickly, and after forty-eight hours it is usually clean and dry. Within four or five days it is possible for the patient to walk with a light dressing in a broad soft shoe.

As the new nail grows, recurrence of abnormal growth must be prevented by frequent observation of the nail and by cutting away any sharp edges which may develop.

RADICAL TREATMENT

Patients are often seen who have had nails removed on two or three occasions, or in whom chronic sepsis has persisted for several weeks, or even months. In such cases a radical cure must be advised. First, the nail must be removed to allow inflammation to subside. Secondly, growth of the nail must be prevented.

Partial excision of the nail bed.—A wedge of nail, nail bed and the exuberant, infected, granulation tissue along the affected side of the nail is widely excised (fig. 5); the resultant defect is allowed to heal by granulation. Recurrence is not uncommon and the operation cannot be strongly recommended. Its main virtue is that it can be performed in the outpatient theatre.

Complete excision of the nail bed.—It is essential that the nail bed should be completely excised, for a troublesome complication of any method of radical cure of ingrowing toenail is the growth of nail remnants. These rudimentary nails form ugly horny excrescences in the area formerly occupied by the germinal matrix of the nail. To avoid this complication, the formative part of the nail bed must be completely excised. The nail fold and the germinal matrix of the lunula must be removed down to bone. The lateral extremities of the nail root are most likely to be incompletely

removed and particular care must be taken to undercut the soft tissues at the base of the nail, in the nail grooves, to reach the germinal matrix. A tourniquet is essential and the operation should be performed in hospital under general anæsthesia.

FIG. 7.—Appearance of the toe after excision of the nail bed and half of the distal phalanx.

Repair of the defect left after excision of the nail bed.—If it is allowed to close by granulation, the defect left after excision of the nail bed is often slow to heal. The covering of the raw area by a partial-thickness skin graft can therefore be strongly advocated (fig. 6). Postoperative healing is rapid and is usually complete in two or three weeks. A graft, the size of a postage stamp, is cut with a razor from the thigh and is sutured to the margins of the raw area on the toe. A thin pad of gauze is firmly applied to the graft by adhesive plaster, to prevent the accumulation of blood or serum under the graft. The patient is kept in hospital until the graft is firmly healed. The cosmetic result of this operation is excellent.

In the operation of hemiphalangectomy, the distal half of the terminal phalanx is 'filleted' out of the pulp of the toe and is amputated. The pulp of the toe can then be drawn over the stump of the phalanx and sutured to the skin at the root of the nail fold. This operation is extremely efficient and produces an excellent functional result (fig. 7). The shortening of the great toe does not affect walking but the stumpy appearance of the toe is rather unsightly and is not always appreciated. It is to be advocated in the elderly, as healing is rapid and hence convalescence is short.

Occasionally, patients return after operations for ingrowing toenail with nail remnants which may be tender and may catch threads in socks or stockings. These rudimentary nails can often be kept under control by rubbing them down with a small file or a coarse dental burr. If they are more troublesome it may be necessary to avulse them under anæsthesia and to treat their bases by excision and curettage.

REVISION CORNER

SINUS ARRHYTHMIA AND SINO-ATRIAL BLOCK

SINUS arrhythmia is undoubtedly the commonest variety of irregular heart action and it is essentially benign in its nature. As it has not infrequently been mistaken for non-benign forms of arrhythmia, it is important that its diagnosis should be beyond doubt.

CAUSATION OF SINUS ARRHYTHMIA

The essential nature of sinus arrhythmia is its close association with respiration. The lessened vagal tone during inspiration acting through the sino-atrial node, leads to a moderate, and occasionally striking, acceleration of the heart rate; and during expiration the heart slows. Holding the breath

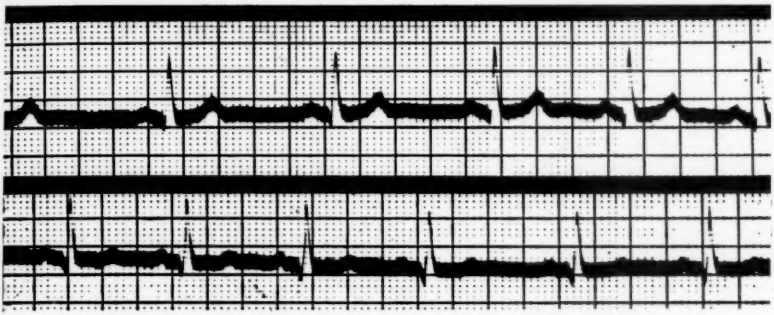


FIG. 1.—A typical example of sinus arrhythmia (leads I and II).

in expiration often leads to further slowing. Phasic variations of rhythm are occasionally found to be independent of respiration. In both these groups it is possible that there is variation of sympathetic as well as vagal tone. Sinus arrhythmia is a common and indeed a normal finding in young people, hence the alternative name juvenile arrhythmia; but it is uncommon in infants. It is a fairly common finding persisting into adult life and such patients seem prone to fainting attacks. Simple sinus bradycardia is often associated with this type of cardiac irregularity; and the fact that inducing rapid action by exercise leads to a temporary disappearance of sinus arrhythmia provides a simple test that should prevent any hasty insistence on prolonged bed rest. Amyl nitrite and atropine will also abolish this variation in the cardiac rhythm.

CLINICAL FEATURES OF SINUS ARRHYTHMIA

The clinical diagnosis can usually be made with every confidence at the bedside, but if there is any doubt at all an electrocardiogram should be

taken. This will reveal normal P waves followed by normal QRS complexes without any delay in conduction, with variation in the length of the diastolic period—the TP interval (fig. 1). In the vast majority of the patients there is no clinical, radioscopic or electrocardiographic evidence of disease. On the

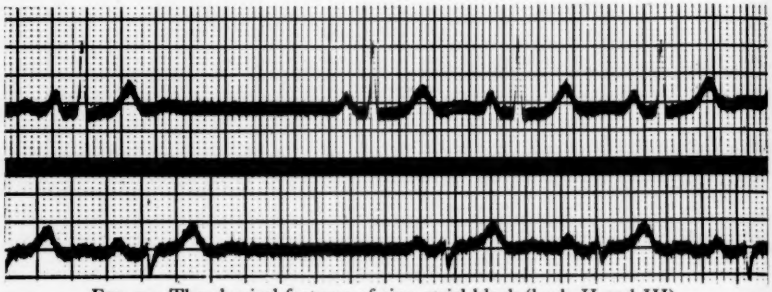


FIG. 2.—The classical features of sino-atrial block (leads II and III).

other hand, sinus arrhythmia has been found present in cases of congenital heart disease and during rheumatic fever; and also in patients undergoing digitalis therapy because digitalis increases vagal tone. It is often observed in patients recovering from an acute febrile illness, such as pneumonia, influenza and rheumatic fever, when there has been marked tachycardia during the earlier phase of the illness, and the same remark is true concerning cases of thyrotoxicosis responding to treatment. Indeed it has been suggested that the appearance of sinus arrhythmia during convalescence is strong presumptive evidence of recovery with reassurance that there has been no permanent myocardial damage.

It has, however, been found that this type of disturbance of rhythm can occur transiently in association with recent myocardial infarction, and in such cases it is assumed that there has been an impairment of the blood supply to the sino-atrial node; there is usually an allied bradycardia and the assessment of the prognosis in such a case should not in any way depend upon the change in rhythm. Digitalis overdosage may induce sinus arrhythmia, and one has seen digitalis 'pushed' in an attempt to control the arrhythmia in the mistaken belief that the case was one of auricular fibrillation. Finally, the appearance of sinus arrhythmia in arteriosclerotic heart disease in the elderly should be regarded with suspicion, and may prove to be a pathological finding.

SINO-ATRIAL BLOCK

In connexion with sinus arrhythmia one must bear in mind its close association with sinus bradycardia where the impulse starts normally in the pacemaker and the heart rate is usually between 45 and 60 per minute. Bradycardia has already been discussed in Revision Corner (*The Practitioner*, 1958, **180,** 625), so that nothing further need be added to the subject in this

note. Sino-atrial block, however, is closely related to sinus arrhythmia, and the presence of both together adds to the difficulty of diagnosis. In this condition a beat is dropped at the wrist whilst the electrocardiogram, instead of revealing an extrasystole, shows that a complete cardiac cycle has been

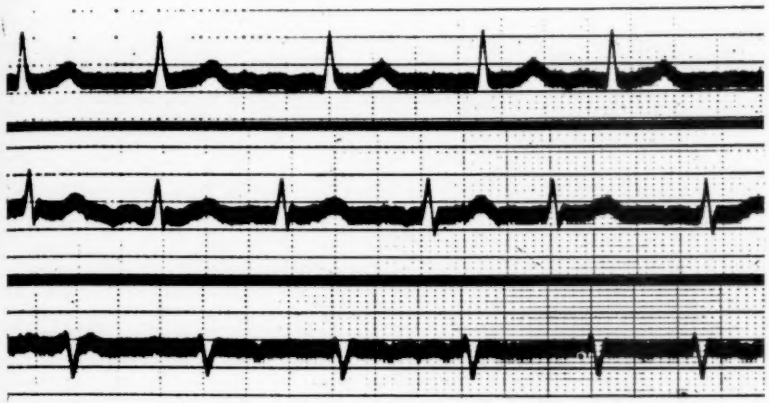


FIG. 3.—Electrocardiogram (leads I, II, III) showing how closely auricular fibrillation can simulate sinus arrhythmia. Note absence of P waves throughout.

blotted out owing to the transient failure of the pacemaker. As a result the whole PQRST complex is absent, leaving a gap, which is nearly, though rarely exactly, twice the length of the normal interval between the beats (fig. 2). As a rule this is a transient lapse, although occasionally it may persist through several cycles—if so, there may be escape beats of nodal or ventricular origin, and during the episode the patient will complain of dizziness and faintness. As a rule there is no demonstrable underlying lesion, but it may occur after an acute illness and it is often associated with the exhibition of digitalis and quinidine; it is also said to follow atrial infarction, but this is rare. Not infrequently pressure on an abnormally sensitive carotid sinus impairs the activity of the pacemaker and may induce arrest for a period long enough to produce unconsciousness. Many examples come to mind:—

The policeman whose 'epilepsy' always came on at about 7.30 a.m. and invariably in the bathroom. The etiology was confirmed by producing marked sino-atrial block (and eventually cardiac standstill) by pressing his carotid sinus, and even more convincing was his demonstration of his shaving technique—it was obvious that he compressed the carotid sinus himself while tightening the skin of his neck, ready for a long steady upward sweep with a cut-throat razor!

Then there was the carpenter bending well down over his workbench to plane some tough oak, and always ending up semiconscious on top of his heap of wood shavings. The advice to discontinue wearing a stiff starched collar and to adopt an open-necked shirt had the desired effect, and enabled him to carry on his work without distress to himself or embarrassment to his fellow-workers.

And finally, there was the motorist having a quick look to the right while rushing the traffic lights at amber . . . he should have worn a scarf!

It is only on very rare occasions that an operation for carotid denervation

is necessary in such patients. These cases of abrupt sinus disturbance are of great importance as they are often regarded as suffering from epilepsy; and it may not be out of place to add here that a similar view had been taken in five of my patients with paroxysmal tachycardia with a particularly dramatic type of onset.

Sino-atrial block is nearly always a harmless condition, apart from the exceptional cases already outlined; and no special treatment is called for once the diagnosis is established by electrocardiography. The most important point in the management of a case is to prevent the patient hearing the full diagnosis: the first part of the name will convey nothing to him but the ring of the second is unmistakably sinister. It may well prove to be the basis of a profound cardiac neurosis—a devil that many months of firm and repeated reassurance may fail to exorcise, especially as the patient may be aware that an 'infallible machine' discovered the 'block'.

CONCLUSION

A word in conclusion about sinus arrhythmia itself. Once the diagnosis is firmly settled no particular line of treatment is necessary and the patient should be reassured and encouraged to lead a full active life. The essential consideration is to make certain of the nature of the arrhythmia in any particular patient (fig. 3). One has known young people kept in bed for a long time 'hoping for the heart to settle down' and the dilemma is aggravated if there is an indefinite history of growing pains and a vague systolic bruit present. Only a comprehensive assessment—clinical, cardioscopic and electrocardiographic, together with erythrocyte sedimentation rate and antistreptolysin O titre estimations—can furnish the answer. Whenever there is any doubt such an assessment should be undertaken *before* deciding to keep the young person in bed for months. The other difficulty presented by sinus arrhythmia is evidenced by patients being referred to clinics with 'auricular fibrillation' and they are often on digitalis already in one form or another. Their symptoms are rarely of cardiac origin, and most of their trouble is the result of digitalis intolerance. Beyond the adolescent stage it can be stated firmly that the main importance of sinus arrhythmia is that its misinterpretation may lead to the diagnosis of a serious pathological disturbance of cardiac rhythm, thus exposing the patient to the risk of an unjustifiable and perhaps prolonged period of 'ill health'.

E. Wyn Jones, M.D., F.R.C.P.
Physician, Liverpool Royal Infirmary;
Physician, Liverpool Regional Cardiac Centre.

NOTES AND QUERIES

Polio Vaccination in Pregnancy

QUERY (from a reader in B.A.O.R.).—A woman in the seventh week of her first pregnancy was recently given 750 mg. of gamma globulin as a protection against rubella at present prevalent in the community. It is desirable that she be also immunized against poliomyelitis at the earliest opportunity. She has already received the first dose of a British polio vaccine, but that was some 9 weeks ago, and, because of lack of supplies, has failed so far to receive the second dose.

Will it be necessary for her to receive both doses of polio vaccine at a 3-4 week interval, or will one further dose be sufficient? Also, will the gamma globulin have any nullifying effect on the antibody response provoked by one or more doses of polio vaccine given within four weeks of receiving the gamma globulin? If a further dose of gamma globulin is deemed advisable, would it be in order to go ahead with poliomyelitis immunization simultaneously?

REPLY.—The gamma globulin prepared from a large pool of blood plasma from adult donors contains variable amounts of antibodies to poliomyelitis as well as rubella viruses. There is always the possibility of some interference with the responses to polio vaccine given within a short interval of an injection.

The immediate concern for this pregnant patient is protection against the rubella prevalent in the community. She has already received one dose of gamma globulin, presumably because she could not provide a reliable history of an attack of the disease. In similar cases, it has been recommended that, when there is more than one exposure at intervals of longer than two or three weeks, a further dose should be given at each contact. As the fœtus does not appear to be endangered by maternal infection after the first four months of pregnancy, however, the practice can cease at that time. After the fourth month, but not previously, attention should be given to further polio vaccination. The effect of the first dose of vaccine given some months before should not have been prejudiced by the long delay in continuing the course. Notwithstanding the injection of gamma globulin, the 'secondary stimulus' type of response to a second dose, given, say, at the end of the fifth month, might even be enhanced by the wide interval between doses of vaccine. Nevertheless, as a two-injection schedule protects at best only 70 to 80 per cent. of persons, a third dose at the end of the seventh month might be considered advisable, if supplies of vaccine permit.

H. J. PARISH, M.D., F.R.C.P.ED., D.P.H.

Parenteral Use of Oxytetracycline

QUERY.—What are the advantages and disadvantages of using oxytetracycline intramuscularly and intravenously, as compared with oral use?

REPLY.—The parenteral use of oxytetracycline is indicated when the patient's condition prevents satisfactory oral administration. This is usually the result of vomiting and the most common indication is peritonitis. Intravenous administration may also be useful in fulminating infections. Special intravenous and intramuscular preparations are available. Intravenously up to 2 g. daily may be given and it is essential that the drug should be well diluted, so that the most satisfactory method is to mix it in an infusion. Intramuscularly a dose of 100 mg. four times daily is satisfactory and should not be exceeded.

The special disadvantages of parenteral use are a tendency to thrombophlebitis if the drug is given intravenously, whilst intramuscular injections may be painful. The chief hazard of a broad-spectrum antibiotic, that of causing an overwhelming infection with a drug-resistant organism, is present whether oral or parenteral administration is used.

KENNETH MACLEAN, M.D., F.R.C.P.

Angioneurotic Œdema in Childhood

QUERY.—I have a ten-year-old boy who is quite healthy except for recurrent attacks of unilateral periorbital œdema, always affecting the right eye. The swelling usually starts first thing on waking but has quite disappeared within twenty-four hours. During the first attack in January he was mildly febrile. In succeeding attacks in February and June he was afebrile. Two white blood cell counts (and differential) have been normal, the first within twenty-four hours of the subsidence of the swelling. The urine has always been normal and physical examination has always proved negative. He has never been abroad or eaten uncooked sausages. I am at a loss to account for the swelling around the eye and would be glad of advice as to methods of investigation and likely diagnosis and treatment.

REPLY.—This is almost certainly a case of angioneurotic œdema. In this condition circumscribed weals arise suddenly in various parts of the body, usually on the face and extremities. Constitutional symptoms are exceptional. The lesions vary greatly in size and

are much larger than those seen in simple urticaria. There is seldom much pain or itching and the child may not be aware of the disturbance. The lesions usually occur on the skin and subcutaneous tissues, less often on the mucous membranes. They persist for one to twenty-four hours or more and recurrences are the rule, the weals tending to reappear in the same situations.

There is undoubtedly some association with conditions of protein sensitization such as urticaria, although this relationship is not clear. Heredity is a factor in some cases, but nervous influences probably play the most important part, thus accounting for the synonym 'vasomotor neurosis'. It is exceptional for an exciting cause to be discovered, but infection, trivial injury and even a special article of diet have apparently been associated with attacks. Spontaneous recovery sometimes occurs; in general, the younger the child the better the outlook.

A very careful history should always be taken and routine sensitization tests be done, in spite of the fact that there is no direct relationship with protein sensitization in the large majority of cases. Treatment with antihistamines is worth a trial though not always successful. Atropine is undoubtedly of value in an acute attack, sometimes as belladonna orally. Adrenaline and ephedrine are also useful. Local soothing lotions may help when itching is troublesome.

PROFESSOR J. L. HENDERSON, M.D., F.R.C.P.

Psittacosis

QUERY.—If one suspects ornithosis in a household, what manifestation of disease may one expect in the family budgerigar or parrot? May the bird be quite fit?

REPLY.—In the epidemic of psittacosis in 1929-30 the signs of fatal sickness in parrots, budgerigars and pigeons were refusal of food, ruffling of feathers, occasional diarrhœa, and a frothy, clear discharge from the nasal orifices. Later it was proved that a large number of birds harboured the virus of psittacosis without any symptoms or signs of ill health and there is no doubt that human infection occurred from contact with these carriers.

PROFESSOR A. P. THOMSON, M.C., M.D., F.R.C.P.

Treatment of Tapeworm Infestation

QUERY.—Can you tell me the latest treatment for tapeworm (*Tænia saginata*) infestation? The patient I have in mind has not responded to male fern, hexylresorcinol, or dichlorophen.

REPLY.—If a full dose, 0.5 g. x 12, of dichlorophen ('anthiphen') has failed and is not considered to be worth a second chance, mepacrine, 1 g. (10 x 100-mg. tablets) for an adult, might succeed. About noon the bowels should be cleared with a soap and water enema and with a dose of saturated sodium sulphate, 60 ml. (2 fluid ounces). When the dose of salts has worked, the mepacrine may be given at once, swallowed with sips of water, the patient staying quietly in bed until the bowels move.

1½ hours after the mepacrine another dose of salts should be given. Two hours later, if the scolex has not been passed, a soap and water enema should be given. The patient may then break the fast according to appetite. Sometimes the worm does not pass for a day or two.

In hospital, after clearing the bowels the patient is usually kept on fluids only on the day of admission, and the mepacrine is given at 5 a.m. next day.

E. L. LLOYD, M.B., D.T.M. & H.

Sexual Frigidity in a Multipara

QUERY.—I have a patient, aged thirty-eight, who has had five children and does not wish to have any more. Her main problem is the fact that she cannot tolerate the thought of sexual intercourse with her husband, nor for that matter is she interested in the opposite sex. The domestic situation has reached a climax and her husband has accused her of unfaithfulness which is quite unjustified. From a psychological point of view I am of the opinion that this attitude could be attributed to her fear of having further pregnancies. I have put this point of view to her but she denies that it has anything to do with it. Can you recommend any solution to this problem in the form of aphrodisiacs as opposed to psychiatric treatment, which the patient refuses to undertake?

REPLY.—This is obviously a problem of grave marital disharmony and treating the single symptom of the wife's apparent lack of libido, even if this were possible, would be useless. Investigation into the reason for the patient's refusal of the normal sex relationship, however, might disclose the underlying causes which are disturbing this couple, and may indicate some constructive line of treatment. It would appear that fear of the unwanted pregnancy is not an outstanding factor in this case, but it is important to know the history of the pregnancies and whether they were planned, the contraceptive methods employed, their reliability and acceptability. Any woman knows that complete abstention from intercourse is the one absolutely reliable means of prevention, and this method is more extensively practised than is always realized.

A consultation with the husband will un-

doubtedly throw a great deal of light on this problem and may show that there is a generalized disturbance in the whole relationship and that sexual difficulty is merely the presenting symptom. Prolonged discussion with both is in itself therapeutic, for the couple themselves disclose to each other and to themselves the real underlying trouble and see the sexual problem in relation to the marriage as a whole. If they both wish the marriage to continue and to reach some harmony in the mutual relationship, then they will be willing to cooperate in talking this out, but the general practitioner will find this very time-consuming. It is obvious that psychiatric help is required here and this woman's refusal may mean that she does not wish the marriage to continue, or may merely indicate a fear, which is very widespread, of what psychiatric treatment may involve. Sympathetic understanding of this fear, and reassurance, may overcome the difficulty, or possibly, if the doctor finds he cannot give the time required, the couple might be willing to discuss the matter at length with a Marriage Guidance Counsellor at the local Marriage Guidance Council, who can work in cooperation with the doctor to clarify the situation.

SYLVIA M. DAWKINS, M.B., B.S.

Ringworm of the Scalp

QUERY.—Attending my school clinic are two children who have had ringworm of the scalp since November 1957, both positive under Wood's light. They have been treated by a skin specialist who has now discharged them as cured, but they remain positive under Wood's light. The specialist has told the parents that the fluorescence under Wood's light will remain for some weeks. I have only had one case of scalp ringworm to treat previously. This case responded to 'tineafax' and I did not regard the child as cured until there was no positive reaction under Wood's lamp.

Does a positive reaction under Wood's lamp always indicate infectivity? What is the best method of treating scalp ringworm in a school clinic? Apparently the specialist did not examine the children under Wood's lamp, but was told by them of my findings when I examined them.

REPLY.—The hairs which fluoresce under Wood's ray should be plucked out with forceps while the child is under the lamp, and examined microscopically for the presence of fungus. If fungus is present the child obviously is not cured. A certain amount of fluorescence under Wood's ray may be caused by ointment used on the scalp and it is incorrect to talk about 'a positive reaction under Wood's lamp' because many substances will cause fluorescence and not all fluorescence noted on the scalp or on hairs is due to the presence of ringworm.

The brief answer to the question as to what is the best method of treating scalp ringworm in a school clinic is that it all depends on what type of fungus is infecting the children. If the inquirer means, what is the best standard ointment to use, most authorities would agree that Whitfield's ointment is preferable to most others.

R. M. B. MACKENNA, M.D., F.R.C.P.

Parosmia Following Head Injury

QUERY.—A patient had a severe head injury 18 months ago. He was unconscious for two days and suffered a fractured skull. Since that time his sense of smell has gone. This does not worry him unduly, but he is very upset by his disorientation of taste. He says that he always has a 'filthy taste' in his mouth and that it becomes worse with food. Most foods taste salty to him. He would prefer to lose his taste rather than continue as he is. Some pus was washed out of his right antrum five months ago, but it is now clear.

Can we do anything to improve his taste or remove it all together?

REPLY.—It is, of course, well known that loss of sense of smell after fracture of the skull distorts taste sense much more in some people than in others. It is possible in this case that the taste mechanism has been to some extent damaged and I think it would be worth while to study this in some detail, possibly in a neurological clinic. Thus, the reaction to a galvanic stimulation of the tongue and to various salty and sweet substances could be analysed and possibly the taste mechanism could be retrained with repeated application of something which did not produce a particularly unpleasant reaction. If, however, the patient is really fond of his food he will never again enjoy it as much as he has in the past.

W. RITCHIE RUSSELL, C.B.E., M.D., F.R.C.P.

Cholesterol and Skin Creams

QUERY.—Is there any advantage in skin creams which contain cholesterol? A patient of mine has recently put this question to me as she has been advised by her beauty-expert friends that a skin cream containing cholesterol improves the texture of the skin.

REPLY.—Cholesterol, and oxidation products such as oxycholesterol, are used to aid emulsification of face creams. They were introduced to obviate such disadvantages as odour and stickiness which may accompany the use of lanolin which was the usual ingredient (Harry, R. G. (1946): 'Modern Cosmeticology' London,

vol. 1, p. 93). Any advantage that may be claimed for cholesterol creams over others probably relates to these emulsifying properties and the pleasant resulting emollient effects on the skin. GEOFFREY HODGSON, M.B.E., M.D.

Vasectomy for Sterilization

QUERY.—What is the present position of vasectomy for sterilization of the male? Has it been universally adopted? Does it impair sexual activity? Is there any record of grave complications, psychic or otherwise, following the operation? What is the technique of the operation?

REPLY.—Vasectomy has not been widely adopted as a contraceptive measure and there is even some doubt about its legality. The technique is simple, namely, exposure of the two vasa through half-inch (12 mm.) incisions at the neck of the scrotum, isolation of the vasa and division of them between ligatures. There are no ill effects and the sexual life is unaltered. Where other contraceptives have failed in the past and sexual relations between husband and wife have become associated with anxiety lest they should fail again the results of vasectomy have been excellent. Successful restoration of the potency of the ducts has been achieved but cannot be guaranteed. The sterilization should therefore be regarded as permanent. It is for the operator to decide when it is justifiable.

KENNETH WALKER, M.B., F.R.C.S.

PRACTICAL NOTES

Treatment of Nephrosis

IN children with pure lipoid nephrosis the addition of nitrogen mustard at the end of a course of hormone therapy increases the number and the duration of the remissions that are obtained, according to C. D. West (*A.M.A. Journal of Diseases of Children*, May 1958, **95**, 498). This conclusion is based upon the findings in a series of 12 cases followed for periods ranging from six to thirty months. Steroid therapy was given for twenty-five days as follows. On days 1 to 14, 150 to 250 mg. of cortisone, or 30 to 50 mg. of prednisone, were given daily. On day 15, corticotrophin injections were started: 60 to 100 mg. of the gel daily. On days 15 to 18 the steroid dose was tapered off. Corticotrophin was then given daily until day 25, and on days 21, 22, 23 and 24, nitrogen mustard was given in a daily dose of 0.1 mg. per kg. intravenously. No serious systemic reactions were noted from the administration of the nitrogen mustard, but vomiting and/or nausea occurred in 10% to 20% of cases. In every case there was a satisfactory diuresis, and in all but one the albuminuria disappeared on the addition of nitrogen mustard to hormone therapy. The longest remission has been two years.

That nitrogen mustard may also be of value in the nephrotic stage of chronic nephritis is suggested by a report by Lo Wen-Chao *et al.* (*Chinese Journal of Internal Medicine*, 1958, **6**, 155). In a series of nine such cases they report complete disappearance of œdema and albuminuria in two cases and improvement in three. In four patients the raised blood pressure also returned to normal figures. The nitrogen mustard was given daily for four or five days, starting with a dose of 1 mg. and increasing this by 1 mg. daily.

Meprobamate in Brain-Damaged Patients

PROMISING results from the use of meprobamate in the symptomatic treatment of patients with organic lesions of the brain are reported by C. H. Carter (*American Journal of the Medical Sciences*, June 1958, **235**, 632). He reports his findings in 105 patients, predominantly children, who were classified in five groups: (i) 47 in whom behaviour problems predominated; (ii) 35 with athetoid cerebral palsy; (iii) 15 with spastic cerebral palsy; (iv) four with paralysis agitans; (v) four cases of 'hyperactivity'. Dosage was adjusted so as to produce 'optimum improvement without drowsiness'. The 'predominant' daily dose was 1,200 mg., ranging from 400 to 3,600 mg. In the majority of cases the drug was administered thrice daily. An analysis of the results shows that more than 80% of the spastic patients and 97% of the athetoid patients showed at least moderate remission of their neuromuscular symptoms. Behavioural problems almost vanished in 57% of the cases and were 'moderately relieved' in 97%. In those cases in which the drug was withdrawn, relapse occurred almost at once, but the condition again responded on renewing treatment and improvement has been maintained for periods up to two years. The only side-effect encountered was drowsiness—in 11 patients. It is reported that 'many patients improved sufficiently to benefit from physiotherapy or psychotherapy for the first time'.

Intramuscular Digoxin

THE intramuscular administration of digoxin is an efficient substitute for intravenous therapy when urgent parenteral digitalization is required,

but has the practical disadvantage of being painful. This is the conclusion reached by E. Fletcher and C. F. Brennan (*Irish Journal of Medical Science*, June 1958, p. 273) as a result of their experience in a series of 20 patients, 18 of whom had uncontrolled auricular fibrillation. The remaining two had 'persistent extrasystolic arrhythmia'. The preparation used was 'lanoxin injection'. A satisfactory therapeutic response (ventricular rate below 90 per minute) was obtained in 15 of the 18 cases of auricular fibrillation within five to nineteen hours of the injection of 1 to 2 mg. irrespective of body weight, age or degree of congestive heart failure. The usual maintenance dose was 0.5 mg. every eight to twenty-four hours. On the basis of their experience the view is expressed that a suitable initial dose in undigitalized patients is 1 mg. of digoxin intramuscularly when the ventricular rate exceeds 120 per minute, and 0.5 mg. if the ventricular rate is less. The concurrent administration of mercurial diuretics may enhance the therapeutic effect of intramuscular digoxin. The only drawback to intramuscular digoxin is pain at the site of injection. This occurred in every case in this series, and increased on repeated injections.

Relaxin

RELAXIN, which together with œstrin and progesterone constitutes the hormonal triumvirate of pregnancy, 'has now reached the same controversial stage in which we found œstrin and progesterone in the early 1930's', according to R. X. Sands (*Canadian Medical Association Journal*, June 15, 1958, **78,** 935). It has been demonstrated in the blood of pregnant women in concentrations which increase gradually to the 38th to 42nd week and it disappears rapidly after parturition. Because of its softening effect upon the cervix it has been used with 'encouraging preliminary results' in the induction of labour in women with a so-called 'unfavourable' cervix, and Ferguson has reported from Miami that it is effective in shortening the duration of labour in primigravidæ and in inducing perineal relaxation. In the field of gynæcology it is claimed to be of value in the treatment of dysmenorrhœa. Following the observation that experimental animals treated with relaxin develop a very loose skin, various clinics in the United States are now investigating its action in scleroderma. Improvement obtained with relaxin is said to be 'over and above that possible with the corticosteroids, and more encouraging than that obtained with sympathectomy alone . . . to date, relaxin appears to have a more favourable effect on the disease than any other form of therapy'.

Pulmonary Osteoarthropathy

'GIVEN a case of lung disease, the discovery of pulmonary osteoarthropathy (periostitis) by x-ray examination of the extremities mitigates against a diagnosis of tuberculosis', according to A. B. Skorneck and L. B. Ginsburg (*New England Journal of Medicine*, May 29, 1958, **258,** 1079) as a result of an investigation of the records of the 390 patients admitted to a tuberculosis hospital during a period of three years. Every patient had the hands, including the distal radius and ulna, and the lower legs x-rayed, as well as the lungs. This revealed three cases of pulmonary hypertrophic osteoarthropathy, none of whom had tuberculosis. The diagnosis was carcinoma of the lung in two and lung abscess in the third. Attention is drawn to the necessity for careful differentiation between clubbing of the fingers, which occurs in many cardiac and pulmonary conditions, including tuberculosis, and osteoarthropathy. The former is usually symptomless, whereas the latter is often accompanied by aching pains. The diagnosis of pulmonary osteoarthropathy is a radiological one, the lesion being a periostitis. Pulmonary osteoarthropathy is always accompanied by clubbing, but clubbing is usually not accompanied by bony changes. Although pulmonary osteoarthropathy occurs in conditions other than carcinoma of the lung, it is suggested that the occurrence of pains in distal portions of the limbs in a patient with a pulmonary lesion should always indicate a careful search for evidence of malignant changes in the lungs. The recorded incidence of pulmonary osteoarthropathy in carcinoma of the lung is between 5% and 10%.

Renal Response to Exercise

'LIMITATION of exercise in patients with impaired renal function or history of acute or chronic parenchymal renal disease' is recommended by E. P. Alyea and H. H. Parish Jr. (*Journal of the American Medical Association*, June 14, 1958, **167,** 807). This recommendation is based upon a study of athletes engaging in lacrosse, football, rowing, running and swimming. In all of these sports between 50% and 80% of the contestants showed albumin, casts and red cells in the urine. In the case of albumin, this was found in between 70% and 80% of cases in all these sports, with the exception of long-distance swimmers in whom it was found in 100% of contestants. Red cells were found in the urine in about 80% of the participants in long-distance running, lacrosse and swimming, and in 50% of those engaging in football and rowing. The duration of the event seemed to play an important part in determining the degree

of the abnormality: in the 1,500-metre swimming race, for instance, the urine was often 'loaded' with red cells and casts. Of the nine long-distance swimmers examined, six had 3+ albumin, three had 6 to 10 red blood cells per high-power field, four were 'loaded' with red cells, and two of these were 'loaded' with casts. The urine usually returned to normal within twenty-four hours. Although the cause for the appearance of these abnormal constituents in the urine after severe exercise is not known, the authors express the view that 'the large amounts of red blood cells, albumin, and casts in the urines of the distance swimmers and track men after severe prolonged exercise make us believe that under such circumstances there is definite renal damage'.

Nocturia in the Elderly

THERE are many cases of nocturia in the male which can be successfully treated by combined therapy with vitamin B_1, œstrogen and a day-time diuretic, according to Sidney Vernon (*Journal of the American Geriatrics Society*, May 1958, **6**, 411). This conclusion is based upon the hypothesis that 'troublesome nocturia in the elderly male may in some cases be due to general ageing of connective tissue, which permits increased hydration of the skin, kidney, and interstitial spaces'. Before embarking upon such medical therapy it is, of course, first necessary to exclude any surgical urological cause for the condition. The recommended dose of aneurine hydrochloride (vitamin B_1) is 25 mg. thrice daily. Œstrogen may be given either as a weekly intramuscular injection in oil, or orally as stilbœstrol—0.5 mg. thrice daily. The recommended diuretic is aminometradine, the diuretic action of which begins within an hour of administration and lasts for eight hours. It is given at breakfast and at lunch.

Isoniazid and Pellagra

THE hypothesis that the administration of isoniazid to undernourished tuberculous patients may induce pellagra is advanced by W. S. Haynes (*East African Medical Journal*, April 1958, **35**, 171). He gives details of six African patients who developed pellagra while under treatment for pulmonary tuberculosis with combined chemotherapy, including low-dosage isoniazid. In one patient pellagra dermatitis was preceded by confusional psychosis, and in three others there was evidence of riboflavine deficiency as well as pellagra. In four of these patients the response to chemotherapy was disappointing. It is suggested that 'in states of nicotinamide deficiency the body cells may grasp and fix the nearly related isonicotinic acid hydrazide which, however, does not prove an adequate substitute for nicotinamide in preventing clinical manifestations of pellagra. Should such a process occur, it would presumably lead to low isoniazid blood levels and a poor therapeutic response'. If this supposition is correct, then it would be advisable to give supplementary vitamin B to patients who are under treatment with isoniazid, particularly in areas where pellagra is known to occur.

Streptonicozid in Leprosy

STREPTONICOZID ('streptohydrazid'), a crystalline compound formed by reaction between streptomycin and isoniazid, 'in a dosage of 5.6 g. a week, given preferably in combination with sulphone therapy, is a method of treatment which we can advocate for the rapid clearing of nasal and buccal lesions, and for those cases which show intolerance to sulphone therapy', according to J. Dreisbach and R. G. Cochrane (*Leprosy Review*, July 1958, **29**, 136) as a result of trials carried out on 47 patients with lepromatous leprosy in Northern Nigeria. Sulphone was given in the form of a 50% solution of solapsone ('sulphetrone'): 3 ml. intramuscularly twice weekly, i.e. 3 g. a week. Erythema nodosum reactions were much less marked than with sulphone therapy, and there was no effect on the white-cell count, although some patients developed anæmia. No toxic reactions, such as drug rashes, hepatitis, renal impairment or central nervous system complications were encountered. Most of the improvement was seen in the first six to twelve months. The over-all results after a period of treatment extending over thirty-two months was: 22% improved and 16% much improved with streptonicozid alone, and 18.5% improved and 33.3% much improved with streptonicozid plus solapsone. The most striking effect, however, was the rapid healing of nasal and buccal lesions.

How to Cough without Abdominal Strain

As a result of personal experience following herniorrhaphy, W. S. Altman (*New England Journal of Medicine*, June 12, 1958, **258**, 1227) recommends the following procedure for reducing to a minimum the abdominal discomfort produced by coughing immediately following an abdominal operation. In the standing position, while leaning forward from the hips, brace the hands and forearms against the washbowl at hip level. By this procedure he found that he could 'cough practically at will, with a minimum of abdominal-muscle discomfort'.

REVIEWS OF BOOKS

Life Insurance and Medicine. Edited by HARRY E. UNGERLEIDER, M.D., F.A.C.P., and RICHARD S. GUBNER, M.D., F.A.C.P. Springfield, Illinois: Charles C Thomas; Oxford: Blackwell Scientific Publications, 1958. Pp. xviii and 994. Illustrated. Price £6 5*s*.

FIFTY-FOUR contributors have combined to produce this compendious review of life insurance practice in the United States. It is based upon a series of lectures organized by the Board of Life Insurance Medicine and is divided into four parts. Part I deals with 'fundamentals of life insurance', part II with 'non-medical aspects', part III with 'medical aspects', and part IV with 'accident and health' insurance. Part III, of course, which runs to practically 500 pages, is by far the longest section and deals in a most comprehensive manner with all the conditions the insurance doctor is likely to encounter. There are even separate chapters dealing with 'histoplasmosis and sarcoidosis', 'coccidioidomycosis', and 'underwriting impaired juvenile risks'. Most of the contributors (45) are associated directly with life assurance societies, whilst the others include such well-known clinicians as Henry L. Bockus of Philadelphia, who writes on peptic ulcer, and Franz J. Ingelfinger of Boston, who writes on benign gastro-intestinal conditions.

Although American practice differs in certain respects from that in this country, the volume will prove a valuable reference book to all who have to give an opinion on such matters—and there can be few physicians today who are not called upon for such a purpose at some time or another.

Heart Disease and Pregnancy. BY C. SIDNEY BURWELL, M.D., and JAMES METCALFE, M.D. Boston: Little, Brown & Co.; London: J. & A. Churchill Ltd., 1958. Pp. xiii and 338. Figures 44. Price 72*s*.

THIS treatise should be to hand in every cardiac clinic in which workers are interested in the fate of pregnant patients with heart disease. The authors have managed successfully to present much factual material, yet at the same time to write with a warmth and humanity which has obviously sprung from a deep understanding of the problems peculiar to the subject. Their conclusions are, in the main, based on an experience extending over six years of 277 patients and 355 pregnancies, seen at the Boston Lying-In Hospital.

A good account is given of the present position of mitral valvotomy during pregnancy, and it is interesting to note that the authors have not advised this operation during pregnancy in any patient, although, of course, they comment on the experience of others. The reviewer has wondered for some time how some workers have produced such large series of valvotomies during pregnancy, and cannot help suspecting that the indication for operation during pregnancy may at times be its feasibility rather than desirability. Even so, never to advise valvotomy during pregnancy seems a little too conservative. One statement in the book is dangerous as it stands, yet it is printed in italics (p. 77): '. . . it is our current position (from which we are prepared to retreat occasionally) that any cardiac patient is entitled to a trial of pregnancy'. This enthusiasm will hardly meet with general acceptance. Some criticism can be made of the balance of the book, in that more than twice the space has been devoted to congenital heart disease than to the whole of rheumatic heart disease, when one remembers that most clinics find that congenital heart disease constitutes only 3% of the patients whereas rheumatic heart disease accounts for about 90%.

Operative Surgery. Vol. VI, VII and VIII. Edited by CHARLES ROB, *M.C.*, M.CHIR., F.R.C.S., and RODNEY SMITH, M.S., F.R.C.S. London: Butterworth & Co. (Publishers) Ltd., 1958. Pp. xiii and 434, xii and 276, xv and 199. Illustrated. Price £5 10*s*. per volume.

VOLUME six of this comprehensive work deals with the hand, amputations, plastic surgery including operations for cancer about the face, and with the operations of gynæcology and obstetrics. All these important topics are covered both clearly and comprehensively; indeed this volume will be of great value to that by no means extinct body of surgeons, the men who must do all the surgery of a large and isolated community, without the help of specialist colleagues. The seventh volume deals with the breast and the genito-urinary system. The eighth volume includes sections on neurosurgery, the eye, and the ear, nose and throat, including the paranasal sinuses and the larynx. Seventy-six authors have shared the responsibility of covering all the operations that are likely to be performed in these regions.

The same plan has been adopted in these as in previous volumes, but in volume VII a few of the illustrations have explanatory captions, and gain in value thereby. In volume VIII the section on neurosurgery describes only those procedures that must often be performed away

from, or before admission to, a fully equipped neurosurgical centre; that on the internal ear, on the other hand, contains accounts of operations that are seldom urgent, and that should never be attempted by any surgeon without prolonged apprenticeship to an acknowledged master.

Circulation. Edited by JOHN MCMICHAEL, M.D., F.R.C.P., F.R.S. Oxford: Blackwell Scientific Publications, 1958. Pp. xxiii and 503. Illustrated. Price 50*s*.

THIS volume constitutes the Proceedings of the outstandingly successful Harvey Tercentenary Congress which was held in London in the summer of 1957. To those who had the privilege of attending the Congress it will be treasured as a memento of a memorable occasion. To those who were not so privileged it will be some solace for an opportunity missed. The introductory 69 pages are devoted to a historical survey by such distinguished authorities as Sir Geoffrey Keynes, Louis Chauvois, John F. Fulton and Kenneth Franklin. The remainder of the book is a review of the present knowledge of the circulation by an international panel including such famous names as those of Claude Beck, Sir Russell Brock, A. Cournand and Gustav Nylin. This is indeed a worthy memento of a great occasion.

Lupus Nephritis. BY R. C. MUEHRCKE, M.D., M.S., R. M. KARK, F.R.C.P., F.A.C.P., C. L. PIRANI, M.D., and V. E. POLLACK, M.B., M.R.C.P.ED. Baltimore: Williams and Wilkins Co., 1957; London: Baillière, Tindall & Cox Ltd., 1958. Pp. 145. Figures 43. Price 24*s*.

THE authors of this interesting monograph take the somewhat unusual standpoint that before the introduction of modern methods of treatment for disseminated lupus erythematosus those who suffered from this malady usually died of 'lupus crisis' or as a result of infection; nowadays, because of the use of corticosteroids and other modern methods of treatment, the patients are usually kept free of symptoms for a considerable time but die of progressive renal failure due to glomerulonephritis. They regard this nephritis as a specific disease of the kidneys which is at present the major complication and the most pressing problem in patients afflicted with disseminated lupus erythematosus. This view is debatable. Nevertheless, the careful discussion of all aspects of 'lupus nephritis' is of considerable interest. The authors describe their extensive investigations (which included renal biopsies) in 33 selected cases. They describe in detail the evolution of renal involvement and correlate the changing clinical state, laboratory data, and renal tests with the pathological changes revealed by biopsy. An interesting section deals with the relationship between L.E. and polyarteritis nodosa, rheumatoid arthritis, scleroderma, dermatomyositis, thrombocytopenic purpura, sarcoidosis and Wegener's granulomatosis. There are 307 references and the illustrations are excellent.

This is a book for the specialist, but is bound to broaden the outlook of all who read it carefully and critically.

Child Health and Pædiatrics. By R. MCL. TODD, M.D., M.R.C.P., D.C.H. London: William Heinemann Medical Books Ltd., 1958. Pp. ix and 238. Illustrations 34. Price 21*s*.

THIS book is intended for 'nurses, health visitors and social workers' and, whilst suitable for the last-named, it is in general rather too superficial for the other groups. There is a satisfactory stress on health prevention and hygiene, running to about one-quarter of the book, and a useful chapter on the handicapped child. The section on growth and development reflects the present-day importance of this subject but it is a pity that American figures are used for standards, especially as up-to-date British figures are now available. The illustrations are mostly well chosen but many would doubt the diagnosis of the child on p. 203—described as 'mongoloid deficiency', itself an undesirable term.

Eat Fat and Grow Slim. BY RICHARD MACKARNESS, M.B. London: The Harvill Press, 1958. Pp. 128. Illustrated. Price 10*s*. 6*d*.

THIS book follows closely the views of Pennington in the United States, supported in part by recent work of Kekwick at the Middlesex Hospital. Pennington supposes that some persons who become obese easily cannot oxidize pyruvic acid and so dietary carbohydrate goes to body fat the oxidation of which in turn is inhibited by the high concentration of pyruvic acid. Therefore obesity can be treated by diets containing unlimited fat of any sort provided carbohydrate is rigidly restricted. The evidence for Pennington's views is slender: the rise in resting blood pyruvate has not been demonstrated; and the work of Mayer, Mann, Passmore and others indicates that obesity is not caused by a lowered basal metabolic rate but by inactivity. The experience of Banting is quoted in support, but the facts given by Pennington and therefore by Mackarness are wrong. Kekwick's interesting results of short-term trials on obese patients need confirmation in longer studies with very careful control of body-water

(since high-fat diets cause loss of water) before they can be recommended for general use.

This slim volume is clearly and brightly written. There are several small errors and some wrong physiology. Most practitioners will probably agree with the reviewer that unlimited dietary fat of any kind, combined with drastic restriction of carbohydrate, is unlikely to lead to loss of weight and may cause ill health on the evidence—admittedly imperfect—at present available.

Homosexuality. Edited by CHARLES BERG, M.D. London: George Allen & Unwin Ltd., 1958. Pp. 415. Price 30*s*.

THIS is a collection of papers (some by Freud and Ferenczi) first published in America, now reprinted in England under the editorship of the late Dr. Charles Berg. It contains lay reports by male and female homosexuals writing anonymously, and by a number of psychoanalytical writers from the first to the present decade of this century. A reprint of a paper by Dr. C. G. Jung forms one chapter. Those who regard homosexuality as a moral crime will not be deflected by these writings. Those who believe that psychiatrists encourage self-pity may find support for their views. And many things are said which can only readily be grasped by those familiar with psychoanalytical language. Yet, for all that, much is said here that is but dimly known, and, uneven as the contributions are, the book is a useful introduction to a subject seldom approached so well. The Editorial Survey is one of the least satisfactory parts and might be omitted. Dr. Oswald Schwarz's paper contains common sense that is worth consideration.

The Matrix of Medicine. Edited by NICOLAS MALLESON, M.D., M.R.C.P. London: Pitman Medical Publishing Co. Ltd., 1958. Pp. xviii and 234. Price 45*s*.

IN many ways this is an important collection of essays of somewhat varying quality and readability. Its main theme is the enormous social and economic loss and personal misery due to preventable and curable disease. It is refreshing in that it shows the social and economic advantages of keeping patients out of hospital. To read it would open the eyes of hospital doctors to how much they do not see or know about medicine. An attractively written summary would enlighten every M.P. on the importance of having an effective medical service rather than a cheap one, and Dr. Marjory Warren's chapter on geriatric care would make every county councillor a lot wiser and more enthusiastic about the welfare services he is supposed to administer. Dr. Cicely Williams, with her experience in WHO, writes scrappily but effectively on food problems all over the world and concludes 'there is more malnutrition through ignorance and prejudice than through lack of available or potential food supplies'. Some chapters seem specially directed to doctors, particularly Dr. Gwyneth Cotterell's contribution on the climacteric and the posthumous essay by Joan Malleson on its social implications. Dr. R. Asher on 'Somatopsychics' makes a trenchant and delightfully readable counterblast to a current fashion 'because I believe the advance of psychosomatic medicine needs checking'. Dr. R. Logan on industrial medicine and Dr. N. Malleson on student health both have interesting and perspicacious comments to make and agree about the comparative uselessness of routine medical examinations.

There are also chapters on nursing, the home care of sick children, the family doctor, mental and chest diseases—all worthy of attention and together making a volume that deserves to be read and acted upon if we are to grasp the possibilities of health that medical science offers mankind today.

Sir Charles Bell. His Life and Times. BY SIR GORDON GORDON-TAYLOR, K.B.E., C.B., F.R.C.S., and E. W. WALLS, M.D., F.R.S.ED. Edinburgh: E. & S. Livingstone Ltd., 1958. Pp. xii and 288. Figures 49. Price 42*s*.

THIS tribute to one of the great names on the roll of the Middlesex Hospital—written by one of its greatest living sons and the present incumbent of the Hospital School's chair of anatomy—will appeal to all who are interested in the history of British medicine. Sir Charles Bell—whose name is still used eponymously for facial palsy and for the long thoracic nerve—was one of the many offspring of the Scottish manse who found his way to London—there to establish an international reputation. Unlike so many of his compatriots he made the return journey in his latter days—to occupy the chair of surgery in his native city for the last six years of his life.

Like so many successful Scotsmen he was a curious mixture of ambition, sentimentality and intolerance, with a searching restless mind that took in the whole of life as his parish. His biographers rightly say that 'a century and more after his death he is remembered as anatomist, physiologist, surgeon, artist and, yes, philosopher too'. Whether they are right in wishing that he had 'confined himself more to his "constant preoccupation", the nervous system', is problematical. The only criticism of this biography is that it scarcely does justice to the

fascinating personality which lay behind this brilliant anatomist and surgeon who lent such lustre to the annals of British medicine. As a critical assessment of his work, however, it is deserving of every praise.

NEW EDITIONS

Psychosomatic Medicine—A Clinical Study of Psychophysiologic Reactions, by Edward Weiss, M.D., and O. Spurgeon English, M.D., third edition (W. B. Saunders Co., 73*s*. 6*d*.).—The first edition of this book had an important influence on the development of medical thought. The new edition is a notable advance on its predecessors in that the intervening years have allowed the authors to develop their ideas much more precisely so that now a great deal of practical help in the handling of individual patients in practice is provided. The work is divided into two sections: the first on general aspects of psychosomatic medicine and the second dealing with special applications to general medicine and the specialties. The first part provides a first-class discussion of the relation between emotion and disease. It should be read by everyone taking any part in medical education, and every experienced general practitioner will read it with delight. The complexity and nature of the subject make it necessary that the second part is less satisfactory as a whole, although certain chapters are notably effective. For example, the practical advice to the migrainous patient will strike every thoughtful doctor as peculiarly apt. The main criticism of the book is that the authors seem deliberately to avoid what is the most important growing edge of psychosomatic thought—the relationship between psychological disturbance and the somatic effect. The book is strongly recommended.

Eye Surgery, by H. B. Stallard, M.B.E., M.D., F.R.C.S., third edition (John Wright & Sons Ltd., 95*s*.).—Several textbooks on ophthalmic surgery, two of them by British authors, have appeared since the war and others have been translated or imported from abroad so that a field hitherto inadequately covered is now perhaps the reverse. The fact that Mr. Stallard's book has reached its third edition in only twelve years is evidence of its success and value. The new edition is considerably larger and more comprehensive, giving a wider choice of the operations available for each disorder. The text is clear and includes much detail. Guides to operative procedures can scarcely be over illustrated—indeed there is a case for a picture book with a minimum of text—and the author has greatly added to his writing by many clear and helpful drawings of his own. Nowadays it is difficult for a single man to produce a good textbook unaided and Mr. Stallard is to be congratulated on producing this enlarged edition with so little outside help.

Handbook of Treatment of Acute Poisoning, by E. H. Bensley, M.B.E., M.D., F.A.C.P., and G. E. Joron, M.D., C.M., F.A.C.P., second edition (E. & S. Livingstone Ltd., 15*s*.), deals primarily with acute poisoning with the emphasis on emergency measures. By means of good selection, the omission of theoretical considerations and the description of only important types of acute poisoning, the authors have produced a very good guide for the general practitioner. This is a Canadian book, and it is rather a pity that the names of the drugs and references to sources of supply have not been 'translated' for the British user. The book can also be useful to the intelligent layman in that it deals with treatment before the arrival of the physician. For the practitioner who wants further information there is a well-selected bibliography. This book should be on the shelf of all casualty departments.

Infant Feeding and Feeding Difficulties, by Philip Evans, M.D., F.R.C.P., and Ronald Mac Keith, D.M., F.R.C.P., D.C.H., third edition (J. & A. Churchill Ltd., 16*s*.).—Three editions in seven years is an indication of popularity. Dr. Mac Keith has been responsible for this third version of a useful and practical book. New views on the physiology of lactation have been incorporated and there are sections on various new diets now available—such as those for phenylketonuria, cœliac disease and galactosæmia. The chapter on practical manœuvres gives a dozen pages of sound advice although the phrase 'do this procedure' is out of keeping with the usual elegance of language (and the charming quotations heading each chapter).

Biochemical Investigations in Diagnosis and Treatment, by John D. N. Nabarro, M.D., F.R.C.P. (H. K. Lewis & Co. Ltd., 25*s*.).—The second edition of this wholely admirable book is most welcome. It is written primarily as a practical guide for hospital residents and registrars and coming from the hand of a skilled physician gives wise guidance on the use of biochemical investigations in diagnosis and control of treatment. Apart from being brought up to date this edition contains an account of isotope techniques, now assuming increasing importance in supplementing biochemical investigations.

The contents of the October issue, which will be a Special Number devoted to 'Advances in Treatment', will be found on page A 118 at the end of the advertisement section.

Notes and Preparations see page 369.
Notes from the Continent see page 373.
Fifty Years Ago see page 375.
Motoring Notes see page A 89.
Travel Notes see page A 93.

NOTES AND PREPARATIONS

NEW PREPARATIONS

'CHYMAR-ZON' is lyophilized α-chymotrypsin in reduced strength suitable for zonulolysis in intracapsular extraction of the lens. Supplied in cartons containing one vial of 'chymar-zon' (100 Armour units) and 2 x 1-ml. vials of Ringer's solution. The preparation is reconstituted with one vial of Ringer's solution, the other vial being provided for irrigation purposes. (Armour Laboratories, Hampden Park, Eastbourne, Sussex.)

'DELTASTAB' injection is a sterile suspension containing 25 mg. of prednisolone acetate B.P. in each ml., and is intended for the treatment of conditions such as rheumatoid arthritis, osteoarthritis, and tennis elbow. The dosage required is stated to be half that of hydrocortisone, which makes it 'particularly advantageous when treating small joints such as those in fingers or toes'. Supplied in rubber-capped vials containing 5 ml. (Boots Pure Drug Co. Ltd., Station Street, Nottingham.)

'TENORMAL' tablets contain pempidine tartrate, which is a ganglion-blocking agent with an action similar to that of mecamylamine but 'having the advantages of being less toxic and less variable in hypotensive effect'. It is intended for the treatment of essential hypertension, both moderate and severe, and of malignant hypertension. It is contraindicated in the presence of glaucoma, pyloric stenosis and uræmia. Supplied in packs of 50 and 500 scored tablets in strengths of 5 mg. (2.5 mg. base) and 10 mg. (5 mg. base). (Imperial Chemical Industries Ltd., Pharmaceuticals Division, Fulshaw Hall, Wilmslow, Cheshire.)

FILM NEWS

Jenny Comes Home (16 mm., colour, sound; running time 30 minutes) is an instructional film on mothercraft for new and expectant mothers and deals with all aspects of baby care, both when the baby is a few days old and when she is six months old. Produced by Eothen Films at St. Thomas's Hospital, with the cooperation of the Royal College of Midwives, the film is available on free loan from Johnson & Johnson (Gt. Britain) Ltd., Slough, Bucks.

FORTHCOMING CONFERENCE

THE *Third International Congress of School and University Health* will be held in Paris in 1959, from July 6 to 8 inclusive. Full details may be obtained from: Comité d'Organisation du Congrès d'Hygiène Scolaire et Universitaire, 13 rue du Four, Paris 6e, France.

RHEUMATOLOGY PRIZE

IN an international competition under the auspices of the Italian Society of Rheumatology, two prizes to the value of 1,000,000 and 500,000 Italian lira, respectively, will be awarded for original and unpublished works on rheumatic diseases. Full details may be obtained upon application to: all'Azienda Autonoma di Cura di Acqui Terme, Piedmont, Italy.

STEROID TREATMENT CARD

BECAUSE of the importance of knowing when a patient is on long-term treatment with steroids, and in what dosage, the Empire Rheumatism Council has prepared a card for issue to such patients, stating the preparation in use and its daily dose. The Council will supply these cards to any physician who might wish to use them. The address of the Council is: Faraday House, 8-10 Charing Cross Road, London, W.C.2.

ROYAL MEDICAL BENEVOLENT FUND

DURING the year ended December 31, 1957, the Fund disbursed a total of £43,942 in grants and annuities, and the annual report emphasizes the need for more funds to meet ever-increasing demands. Immediate help is given in urgent cases and all deserving applicants are treated impartially. A special appeal is made for 'covenanted' subscriptions (seven-year covenants) as these are of greatly increased benefit to the Fund without further cost to the subscriber. The address of the Fund is: 1 Balliol House, Manor Fields, Putney, London, S.W.15.

THE KING'S FUND

INTELLIGENT eclecticism is again the keynote of the annual report of King Edward's Hospital Fund for London. During 1957, expenditure amounted to £323,955. Three examples may be quoted of the variety of its benefactions. Sixteen of the independent hospitals outside the National Health Service have been allotted grants, including £5000 for the French Hospital, £1,300 for the British Hospital and Home for Incurables, and £6000 for the Lingfield Hospital School for epileptic children. The recent interest in the application of work study to hospital management is being encouraged by a grant of £5000 towards the cost of a three-year experiment in work study at the Westminster Hospital. Hospital gardens have for long been a specialty of the Fund, and during 1957 grants of £2,810 have been made to six hospitals for this purpose.

EMERGENCY BED SERVICE

THE increase in the number of maternity cases being dealt with (1,600, compared with 950 in 1955) is now causing 'some anxiety', according to the annual report of the London Emergency Bed Service for the year ended March 31, 1958. Apparently many antenatal clinics now instruct patients, for whom beds cannot be booked, to call in their doctor or midwife when labour starts and ask him or her to arrange admission through the Emergency Bed Service. This is described as a 'most unsatisfactory procedure' and 'unfair to the patient who suffers unnecessary anxiety and inconvenience'. In a number of cases it has resulted in the baby being born in the ambulance or in unsuitable conditions at home. Either there are inadequate beds to meet the needs of the population or those responsible for bookings are not being sufficiently selective in arranging them. Whatever the explanation, the situation is described as 'one that calls for urgent remedy'.

ULSTER GENERAL PRACTICE

DURING the first ten years of the National Health Service the number of doctors in partnership practice in Northern Ireland rose from 123 to 353. The number of dual partnerships rose from 54 to 142, and the number of triple partnerships from five to 23. The total number of doctors in practice as principals is 737. The average number of persons on a doctor's list is 1,889. These figures are taken from the recently published tenth annual report of the Northern Ireland General Health Services Board, which covers the year ended March 31, 1958. A total of 63 doctors attended the five refresher courses for general practitioners organized during the year.

SOCIAL SECURITY RECIPROCITY

THE Convention on Social Security between the United Kingdom and Yugoslavia comes into force today (September 1). The Convention covers cash benefits provided by the two countries for unemployment, sickness, maternity, old age, widowhood, orphanhood, industrial accidents and diseases, death and family allowances. In addition, medical benefits provided under the Yugoslav Health Insurance Scheme will be available in Yugoslavia to all persons insured under the United Kingdom National Insurance Scheme and their dependants on production of a certificate of British Insurance obtainable from: The Ministry of Pensions and National Insurance, Overseas Group, Newcastle on Tyne.

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

THE *Journal of the American Medical Association* has just celebrated its 75th birthday with a special issue containing contributions from many of the leading citizens of the United States, including Mr. Walt Disney, Mr. J. E. Hoover, the Director of the F.B.I., and Mr. John Steinbeck. It is introduced by a letter of congratulation from President Eisenhower. The colossus of medical journals (its circulation exceeds 180,000) carries with it the best wishes of all its contemporaries as it sets forth on the final lap towards its centenary.

THE COST OF INFLUENZA

WHAT is described as 'the biggest influenza epidemic since the National Insurance Scheme began' brought new claims for sickness benefit in 1957 up to the record figure of 9½ million, according to the annual report of the Ministry of Pensions and National Insurance for 1957. The epidemic is estimated to have cost the National Insurance Fund £10 million. Analysis of the available data suggests that one in eight of the 20 million people insured for sickness benefit may have had influenza.

CARCINOGEN IN CIGARETTE SMOKE

A SUBSTANCE chromatographically identical with 1,2,3,4-dibenzopyrene, a potent carcinogenic agent, has been isolated from cigarette smoke by M. J. Lyons, of the Cancer Research Department of the Royal Beatson Memorial Hospital, Glasgow [*Nature* (*Lond.*) 1958, **182,** 178]: 1.6 micrograms were recovered from 100 cigarettes of average weight 1.1 g. smoked to a stub length of about 1.5 cm. Small quantities were also detected in petrol and the exhaust products of diesel engines, but not in a sample of general urban atmospheric soot. 'Thus', it is concluded, 'it would appear that the urban dwelling cigarette smoker has an exposure to 1,2,3,4-dibenzopyrene in a concentration not realized by his non-smoking neighbour'.

SMOKING AND LUNG CANCER

FURTHER evidence that the genotype exercises a considerable influence on smoking habits is adduced by Sir Ronald Fisher [*Nature* (*Lond.*), 1958, **182,** 108] from a study of 51 monozygotic twins and 31 dizygotic twins in Germany. Of the former, 76% were alike in their smoking habits (e.g. 22 pairs both cigarette smokers, two pairs both cigar smokers), compared with only 49% of the dizygotic pairs. Such genotypically different groups, it is said, 'would be expected to differ in cancer incidence'. Further, only if smokers were genotypically homogenous could causation of cancer of the lung by cigarette

smoking 'be confidently confirmed' from the association observable between them.

DRUG ADDICTS

Of the 359 known addicts to manufactured drugs in the United Kingdom in 1957, 70 were doctors, two were dentists, 15 were nurses and one was a pharmacist. Morphine leads the list with 149 addicts, pethidine coming next with 74. Diacetylmorphine claimed 52 addicts, methadone 20, and three were addicted to levorphanol. Drug addiction is not compulsorily notifiable in the United Kingdom, but 84 new cases were reported in 1957. As judged by seizures by H.M. Customs. illicit traffic in narcotic drugs showed no significant change in 1957, apart from the amounts of opium and cannabis. The amount of opium seized was only 5.3 kg. compared with 54.2 kg. in 1956, whereas the amount of cannabis seized—237.2 kg.—was more than double the quantity seized in 1956.

INCIDENCE OF OLD AGE

In European countries the population percentage of persons aged 60 years or more ranges from 22.9% in Monaco to 6% in Turkey. In England and Wales the figure is 15.9%, whilst Scotland is a little lower at 14.4%. Ages for retirement, or pension or old age benefits, for men range from 55 in Argentina to 70 in Canada, Ireland and Norway. In some countries pensionable age varies with the job, whilst in Belgium, France and the U.S.S.R. workers retire earlier from certain heavy jobs.

CHOLERA EPIDEMIC

The cholera situation in Asia is the most serious in years, according to a WHO report. In India, East Pakistan, and Thailand 48,722 cases, with 20,685 deaths, were recorded during the first seven months of the year.

WHAT PRICE AN M.B.?

The current cost of a medical training, as judged by London figures, is between £2000 and £2,500, according to an analysis published in the *Financial Times*. This includes £1,925 for maintenance, and £50 for books and equipment. Another £800 has to be added to those who take a Cambridge or Oxford degree. It is noted that about 75% of medical students now receive some assistance from either a public or private award towards this expense.

TUBERCULOSIS IN HUNGARIAN REFUGEES

Of the 15,500 Hungarian refugees remaining in this country, only 7000 have been x-rayed, and the incidence of tuberculosis in this group is at least 8 per 1000 according to a report issued by the Joint Tuberculosis Council (*Tubercle* (*Lond.*), 1958, **39**, 187). The view is expressed that 'it would appear to be a reasonable assumption that the incidence of tuberculosis in Hungarian refugees is at least twice and may be thrice that usually found in recent British mass radiography surveys' and it is estimated that the number of active cases still undiagnosed is probably between 50 and 100.

It is noted that routine radiography of refugees was not undertaken on arrival in this country and that initiative towards this end was discouraged by the Ministry of Health until examination of a sample of refugees revealed an incidence of tuberculosis of 18 per 1000. It is urged that 'routine radiography of such refugee groups is an essential safeguard for their own health as well as for that of the public'.

CONGENITAL MALFORMATIONS AND MATERNAL AGE

Over 2% (2.1%) of the 1,041 children born to the 1,030 mothers aged 42 or more, who had their confinements in two obstetric wards in Stockholm and Uppsala during 1946-55, were mongols, according to J. A. Boök *et al.* (*Nature* (*Lond.*), 1958, **181**, 1545). The total number of congenitally abnormal children was 47, which gives an average risk of 4.5%. The malformations consisted of 22 cases of mongolism, two cases of anencephaly, six cases of gastro-intestinal abnormality, 10 cases of deformities of bones, muscles and skin (including five cases of congenital clubfoot), seven cases of cardio-vascular abnormality. Except for anencephaly the differences from the average incidence of congenital malformations was statistically significant. Although the mothers concerned constituted only 1.5% of the total number of mothers confined in these two wards during the period of observation, they contributed 5.1% of the total of malformed children during the period.

PUBLICATIONS

The Compend, compiled by W. Hetherington, F.P.S.—A second addendum has now been published to the 'compendium of ethical proprietaries used in medicine and pharmacy'. This incorporates changes which have arisen since publication of the first addendum in 1956, and includes monographs on approximately 220 new products. (John Wright & Sons Ltd., price 5*s*.)

The Determination of the ABO and Rh(D) Blood Groups for Transfusion, Medical Research Council Memorandum No. 36, is a revision of War Memorandum No. 9. It is a comprehensive and authoritative review of the subject which will be

appreciated by all concerned with blood transfusion. (H.M. Stationery Office, price 3*s*. 6*d*.)

Expert Committee on Addiction-Producing Drugs, Eighth Report, WHO Technical Report Series No. 142, deals, amongst other items, with the development of methods for the evaluation of addiction liability and the present position with regard to the misuse of 'tranquillizing drugs'. (H.M. Stationery Office, price 1*s*. 9d.)

The Medical Practitioner's Handbook provides a guide to conditions of practice in the United Kingdom. It will be of particular value to the young practitioner in helping him to unravel the intricacies of general practice. (British Medical Association, price 12*s*. 6*d*. (10*s*. for members of the B.M.A., 5*s*. for final-year students and graduates within the first three months of qualifying).)

Religious Doctrine and Medical Practice, by Richard Thomas Barton, M.D., F.A.C.S.—Illness with its realization of our mortality can conjure up vividly the religious tenets instilled in childhood, even if they have been neglected for half a lifetime: and a wise doctor must see to it that there is no avoidable conflict in his patient's mind. Yet how many of us give a thought to this until we suddenly find the harm is done? Dr. Barton's book is a practical handbook by which such errors may be avoided. He writes easily and concisely, and tabulates the main religions with regard to their teaching on the cause of illness, health laws and diet, and the role of the physician. Apart from its obvious practical use, it is a fascinating guide to the many religions of the world today. (Blackwell Scientific Publications, price 27*s*. 6*d*.)

Psychiatry in the Modern World, by E. B. Strauss, M.D., F.R.C.P., consisting of several articles published in the *Sunday Times*, represents another step towards informing the public about the clinical psychiatrist and his work. A wide range of subjects, including symptomatology and treatment of the neuroses and psychoses, is covered, giving the reader an understanding of a good deal of elementary psychology and psychiatry. Considering the extreme limitations of space, the author artistically and refreshingly avoids dramatic presentation, controversial issues and dogma. A minor blemish is the use of the term 'cyclophrenia' in such an elementary setting. Although this pleasant book is intended for the intelligent general reader, the broad yet personal approach makes it an interesting introduction for the student. (Michael Joseph Ltd., price 8*s*. 6*d*.)

Parents' Handbook contains notes for parents on the home care of children handicapped by cerebral palsy and includes advice and illustrations on the use of simple play material and adapted furniture. (British Council for the Welfare of Spastics, 13 Suffolk Street, London, S.W.1, price 2*s*. 6*d*.)

Elizabeth Garrett Anderson, by Jo Manton, is the latest addition to the admirable 'Lives to Remember' series. In simple straightforward language it tells the fascinating story of the pioneer of British women doctors. The author has caught the atmosphere of the period and conveys vividly yet without any exaggeration the difficulties which Elizabeth Garrett had to encounter and the consternation which her success caused in orthodox medical circles. It will appeal to all senior schoolgirls, and particularly to those who are considering medicine as a career. (A. & C. Black, price 6*s*. 6*d*.)

London Medical Scheme gives full details of the scheme which was introduced in 1953 and is now recognized internationally as a model of its kind. Its aim is threefold: (a) To prevent any boxer competing who is not physically fit to box. (b) Not to prevent any boxer from competing who is physically fit to box. (c) To ensure that an injured boxer has completely recovered before starting to box again. A copy of this pamphlet should be in the hands of every doctor who has any association with boxing. (London Amateur Boxing Association, price 1*s*.)

Doctor at Stalingrad, by Hans Dibold, is the tragic tale of the sick German prisoners of war who were trapped in the Stalingrad net. The author is an Austrian doctor serving in the German army, who was also taken prisoner, and in this book he tells of his experiences. It is a gruesome tale, but will be read with interest by doctors. Even they will wonder how any survived the subterranean existence described in the first few chapters. (Hutchinson, price 16*s*.)

OFFICAL PUBLICATION

Report of the Medical Research Council for the Year 1956-1957, as in recent years, is largely devoted to reviews of various aspects of medical research. This year the subjects covered include 'the architecture of a protein molecule', 'the spinal cord in poliomyelitis', 'the mechanism of fever', 'experimental leukæmia', and 'genetics of eye disease'. All these reviews are admirably written and will appeal to the discriminating reader. (H.M. Stationery Office, price 13*s*.)

NOTES FROM THE CONTINENT

BELGIUM

Cardiovascular surgery.—An interesting development in experimental cardiovascular surgery is reported by Castro Villagrana and his colleagues who have demonstrated in the dog that it is possible to produce a competent aortic valve from the intima of the aorta. Histological studies have shown that the reconstructed valve is viable and capable of functioning efficiently for long periods of time An even more interesting development is that of De Weese and Hunter who have evolved a method of inserting in the inferior vena cava filters which will entrap emboli. In dogs, it is claimed, these intravenal filters are well tolerated, do not interfere with blood flow, and produce no delayed sequelæ. It is suggested that such filters might replace ligature of the inferior vena cava as a means of preventing pulmonary infarction from emboli in the veins of the lower extremities. A third development in this field is the report of Coon and his colleagues that radioactive cobalt is an effective means of sterilizing aortic homografts. They claim that the alterations produced in the graft by this method are comparable to those produced by other methods of sterilization.

Total gastrectomy.—A modification of Boerema's method for total gastrectomy, to prevent jejunoœsophageal reflux, has been described by Ch.C. Henry. This consists of forming a jejunal pouch and anastomosing the upper end to the œsophagus and the lower end to the duodenum. This seems to form an efficient 'gastric reservoir' as indicated by the fact that a well-defined air bubble can be demonstrated in it radiologically. Further, it is claimed that patients who have this operation develop a sensation of hunger—a sensation which disappears after operation for total gastrectomy in which no such 'reservoir' is left behind.

'Chemical hypnotherapy'.—'Chemical hypnotherapy' is the term used by P. Divry and his colleagues, of the Psychiatry Clinic of the University of Liège, to describe their method of treating various neurotic and psychiatric states. It takes one of three forms or 'cures':—(a) The 'potentiated sleep cure', in which barbiturates and chlorpromazine are used. (b) The 'neuroleptic cure' in which either chlorpromazine or reserpine is used, with the addition of promethazine. (c) The 'tranquillizing cure', in which either meprobamate or methylpentynol carbamate is used. The first of these is used for treatment of the neuroses, the second for the psychoses, and the third for anxiety and obsessional states. They claim that side-effects are rare. In a series of 353 cases there were seven cases of digestive complications, two of eczema, two of 'cardiovascular collapse', and two of confusional states.

Corticotrophin and delirium tremens.—Dr. L. Massion-Verniory and his colleagues have reported to the Belgian Society of Mental Medicine an interesting case of delirium tremens which had proved resistant to various forms of treatment, including aneurine and various neuroplegics. They then gave him an intravenous injection of 20 units of corticotrophin. Within 2½ hours there was a marked improvement in his condition, leading on to complete recovery.

Insulin and glucose.—Bastenie and his colleagues have shown that in normal individuals the ingestion of glucose is followed by the liberation of insulin which can be demonstrated by measuring the coefficient of assimilation of glucose or by measuring the plasma insulin action in the rat. This liberation of insulin, on the other hand, does not occur in diabetics. They have also shown that the rapid intravenous injection of glucose does not stimulate any secretion of insulin as judged by these two tests. It is suggested that this apparently paradoxical state of affairs is due to the fact that the duration of hyperglycaemia following the rapid intravenous injection of glucose is so short that it is unable to produce a measurable increase in the output of insulin.

Birth-rate and perinatal mortality.—The annual increase in population in Belgium is around 40,000—the resultant of 150,000 births and 110,000 deaths. An analysis of these figures shows that, compared with other countries, the death-rate in Belgium (12.2 per thousand) is on the high side, whilst the birth-rate (16.7 per thousand) is on the low side. The relatively high death-rate is associated with the ageing of the population, and it is noted that up to 1940 this was associated with a fall in the birth-rate. Since 1940, however, the birth-rate has remained fairly constant around 17 per thousand.

The maternal mortality rate is falling steadily, particularly among older women. The infant mortality rate is also falling but, as in other countries, there is concern at the fact that this improvement is least in the immediate postnatal period: i.e. during the first five days of life. When the perinatal mortality is added to the fœtal mortality, the figure of 37 per thousand is attained.

FRANCE

Gargoylism.—In reporting four cases of gargoylism, or as it is still known on the Continent, Hurler's disease, Maurice Lamy and his colleagues review the records of 269 cases reported in the literature. They note the predominance of males—178 boys and 91 girls—and classify the condition into two groups. The first includes all the females and two-thirds of the males. It is characterized by a high incidence of corneal opacities, but deafness and cardiac abnormalities are rare, and the disease runs a fatal course within a few years. Transmission in this group is of the autosomal and recessive type. The second, rarer, group accounts for about one-third of the male cases. Here the corneæ are always clear, but there is a higher incidence of deafness and cardiac abnormalities. Although always fatal, it runs a much slower course than the other group and the victims often survive into adolescence—and even early adult life. The transmission of this group is recessive and sex-linked.

Cerebral angiography.—J. Avet has analysed the records of 1000 cerebral arteriographs carried out in Lyons between March 1953 and June 1956. He emphasizes the need for a rigorous technique such as that which has been used in every case in this series. The procedure was carried out on outpatients and no premedication was used except in the case of children and nervous adults. He used a trocar 7 cm. long and 1 mm. in diameter, with a short bevel and mounted direct on a syringe. No local anæsthetic was used. The radio-opaque substance used was diodone and acetiodone, in two injections of 4 to 5 ml. Side-effects have been minimal. Only once has he seen a hæmatoma in the carotid sulcus, and that was in a case of bilateral angiography. There were no cerebral accidents in the series, and this is attributed to avoiding the use of too large or too concentrated a solution. In five cases conjunctivitis developed in the eye on the injected side the morning following the injection. The method was successful in 30% of cerebral tumours and 38% of meningiomas. It was of least value in the localization of metastases. Its outstanding value was in the case of closed brain injuries, and in Avet's opinion angiography is the most precise method of detecting and localizing such lesions.

Meningeal hæmorrhage in premature infants.—Among the 500 infants weighing less than 2.1 kg. born at the hospital for premature infants in Marseilles during a five-year period there were 75 cases of meningeal hæmorrhage, representing 15% of all the cases. In 70% of cases the condition proved fatal, and this condition was responsible for 51% of all deaths among these 500 premature infants. An analysis by P. Giraud and his colleagues of the case-records, including necropsy records in 59 cases, shows that this bleeding was not the result of rupture of a large vessel or tearing of the dura mater. It was due to oozing of blood from the pia mater, choroid plexus and vessels of the walls of the ventricles, associated with cerebral œdema. Clinically, signs of respiratory diseases (cyanosis, dyspnœa and apnœa) occurred in 71% of cases and were more common than neurological signs (e.g. convulsions) which occurred in only 25% of cases, or disturbances of temperature control. Lumbar or cisternal puncture is of little value in diagnosis. Whilst birth trauma is undoubtedly often a factor, the Marseilles workers lay more stress on the degree of prematurity and particularly the prematurity of the vasomotor system. The basis of treatment is careful resuscitation, analeptics such as lobeline, and sedatives such as phenobarbitone and chlorpromazine. Blood transfusion must be used with caution, and lumbar puncture is more likely to be harmful than helpful. Cortisone occasionally seems to be of value. The only sound therapy, however, is prevention in the form of reducing the incidence of prematurity.

Cor pulmonale.—Four cases of chronic cor pulmonale due to thrombosis of the pulmonary artery have been reported by P. Fortin and his colleagues. There is rarely any evidence of pulmonary embolism, the condition following some acute pulmonary infection ushered in by dyspnœa, which may be insidious in onset, or takes the form of pulmonary œdema or an asthmatic attack. The onset of heart failure may either be insidious or accompanied by transitory episodes of acute cor pulmonale. The physical signs are a rapid pulse, which may be regular or irregular, gallop rhythm (usually presystolic), accentuation of the pulmonary second sound and usually an apical systolic murmur. The blood pressure is usually normal. Later, signs of right heart failure develop: a painful enlarged liver with hepato-jejunal reflux, œdema of the legs, and, rarely, ascites. The venous pressure is always raised. The electrocardiogram shows right ventricular preponderance, and radiological evidence of enlargement of the right side of the heart is always present. The diagnostic features are the development of right heart failure without any evidence of left heart failure or of thrombo-embolic phenomena, together with pulmonary hypertension, normal capillary pressure and decreased cardiac output. The only therapy is preventive—by the long-term administration of anticoagulants.

THE PRACTITIONER

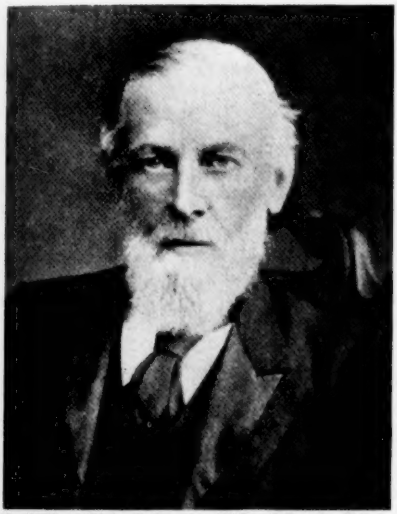
Fifty Years Ago

'Nations have recently been led to borrow billions for war; no nation has ever borrowed largely for education. Probably no nation is rich enough to pay for both war and civilization. We must make our choice; we cannot have both'.—Abraham Flexner: *Universities.*

SEPTEMBER, 1908

'WE are now comfortably settled in our New Building . . . 2 Howard Street, Strand, London, W.C.'

Referring to an appeal for money 'for the purposes of medical education' recently made by the President of the Royal College of



Sir William Richard Gowers, M.D., F.R.C.P., F.R.S., (1845-1915)

Surgeons of England (Sir Henry Morris, Bt.) in *The Times*, the Editor writes: 'The interests at issue are no narrow professional interests, but also concern the entire community of actual and potential patients; for every doctor imperfectly instructed in his science and art may be, at any time, a public danger . . . Medical education is more costly than it used to be, owing, among other causes, to the increasing employment of expensive methods and apparatus. In the second place, many hospitals have lost a certain proportion of their subscribers as the result of the hostile agitation of the anti-vivisectionists, to whose extravagant demands they most properly refuse to make any concessions. In the third place . . . the managers of the King's Hospital Fund, guided by the advice of a committee on which the medical profession was inadequately represented, have decided to withhold grants from all hospitals which devote any portion of their income to the maintenance of their medical schools. Hence a critical condition of affairs, calling urgently for remedial measures preferably in the form of subscriptions to hospitals, earmarked for educational purposes'.

On the subject of 'Preliminary Science' 'Notes by the Way' remark: 'One of the points taken against the medical education given at hospitals needs to be met. Much of their money, it is urged, is spent in teaching "preliminary science", which might just as well be taught elsewhere. The system has been condemned as "wasteful and extravagant"; and it has been maintained that the medical schools should confine themselves to clinical instruction, the cost of which might be covered by the students' fees. The argument may have a plausible ring in the ears of laymen; but it is not really convincing. Science is a large subject. A man may know a great deal of science, and yet not know the right science for a particular purpose'.

The opening article in this issue, 'Malignant Obstruction of the Œsophagus', is by Lawrie McGavin, F.R.C.S., Lecturer on Clinical Surgery in the London School of Clinical Medicine: 'As to the treatment of this condition; it may as well be said at once that it is in the highest degree unsatisfactory, since, in the present state of our knowledge, a cure is out of the question. But much may be done to relieve the patient's sufferings, although it is doubtful if the prolongation of life, in such circumstances, is desirable from the patient's point of view'. Lawrie Hugh McGavin (1868-1932) was a pioneer in filigree implantation for hernia and wrote a successful novel, 'The King's Jester'.

Arthur J. Hall, M.D., F.R.C.P., Lecturer in Practical Medicine, University of Sheffield; Physician, Sheffield Royal Hospital, takes for his subject 'Difficulties of Diagnosis': 'In making a diagnosis, we are necessarily limited, by the existing state of general knowledge, to such arbitrary divisions or pigeon-holes as are currently accepted by the medical thought of the day. From time to time, these pigeon-holes have to be altered to suit the progress of knowledge; it may be that they have to be further subdivided, or it may be, on the other hand, that some two or three have to be joined together into one . . . But whilst the pigeon-holes remain

much the same as they were in our younger days, there comes to each of us a time, when we feel a sense of dissatisfaction with these arbitrary and, sometimes, apparently useless, subdivisions of the textbook. So many of the cases, seen in private practice, seem to be the exceptions which prove the rule, rather than the typical cases which used to be so common in our student days! Such a sense of dissatisfaction is not only natural but, I think, a healthy sign of personal progress'.

T. Crisp English, F.R.C.S., Senior Assistant Surgeon to St. George's Hospital, discusses 'Cancer of the Breast; Indications for Operation'; R. P. Rowlands, M.S., F.R.C.S., Surgeon in charge of the Orthopædic Department, Guy's Hospital, describes 'The Treatment of Wry-Neck by Lengthening the Sterno-Mastoid'; and H. T. Hicks, F.R.C.S., Gynæcologist to the Derbyshire Royal Infirmary, deals with 'Pyelitis during Pregnancy'.

Fourteen books are reviewed this month. 'The Border-Land of Epilepsy' by Sir William R. Gowers is described as 'a very welcome addition to the literature of medicine . . . of special use to the general practitioner, who has had, till now, nowhere to turn for reference when confronted with one of these indefinite cases'. Sir William Richard Gowers (1845-1915), whose name is well known to every medical student through 'Gowers' tract' and 'Gowers' mixture', was elected registrar at the National Hospital for the Paralysed and Epileptic in 1870, assistant physician three years later, and physician in 1880. One of the first articles he wrote, 'On the influence of posture in "pre-systolic" cardiac murmurs', was published in *The Practitioner* in 1873. A great pioneer in neurology, he wrote a 2-volume 'Manual of Diseases of the Nervous System' (1886), which 'became known to the neurological world as a cornucopia wherein treasures could be sought and gathered' (Macdonald Critchley). Of his 'Borderland of Epilepsy' *The Lancet* (1949, i, 1108) said that it 'would have sufficed to keep him in the front rank long after his lectures and demonstrations had been forgotten'.

'Surgical Emergencies' by Percy Sargent 'is a capital book, clear, concise, and suitably dogmatic . . . Embodying, as it does, the teaching and practice of one of our great surgical schools, the advice given is thoroughly trustworthy and sound'. 'Surgery: its Principles and Practice', edited by W. W. Keen, Vol. I, 'deserves little else than praise'.

'Practical Notes' describe 'Cammidge's C Reaction for the Diagnosis of Pancreatitis and Other Diseases of the Pancreas', which 'claims to get *positive* results in all cases of pancreatitis, *negative* results in three-quarters of all cases of malignant disease'.

W. R. B.

ST. ANDREWS HOSPITAL, NORTHAMPTON

FOR NERVOUS AND MENTAL DISORDERS

President—THE EARL SPENCER

Medical Superintendent—THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

This Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders, or who wish to prevent recurrent attacks of mental trouble; temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, biochemical, bacteriological and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE

This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods; insulin treatment is available for suitable cases. There is an Operating Theatre, a Dental Surgery, an X-Ray Room, an Ultra-Violet Apparatus, and a Department for Diathermy and High-Frequency treatment. It also contains Laboratories for biochemical, bacteriological, and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit-growing.

BRYN-Y-NEUADD HALL

The seaside house of St. Andrews Hospital is beautifully situated in a Park of 330 acres, at Llanfairfechan amidst the finest scenery in North Wales. On the north-west side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change, or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses, and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, &c.

For terms and further particulars apply to the Medical Superintendent (Telephone: No. 4354, three lines, Northampton), who can be seen in London by appointment.